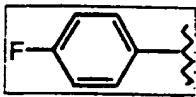
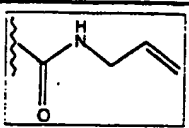
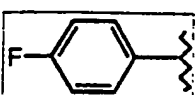
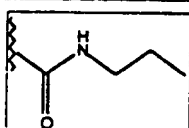
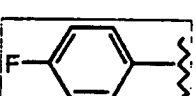
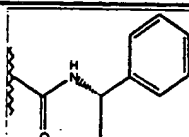
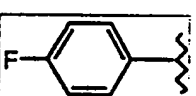
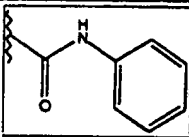
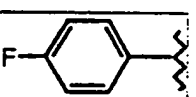
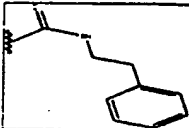
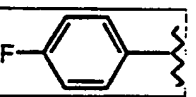
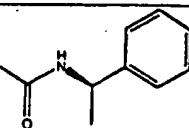
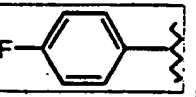
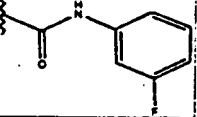
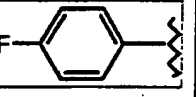
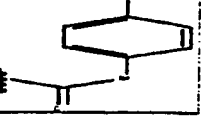
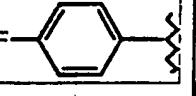
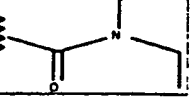
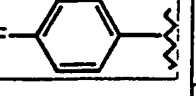
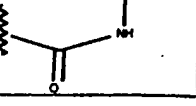
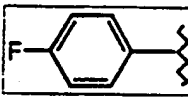
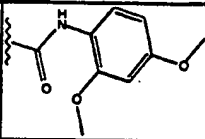
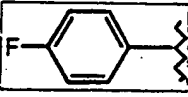
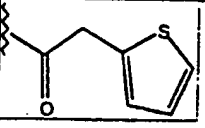
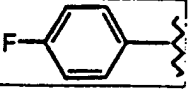

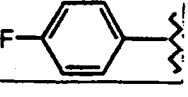
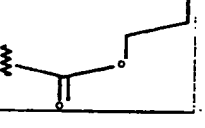
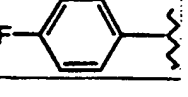
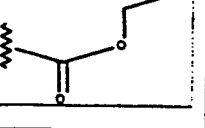
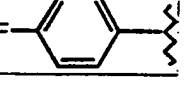
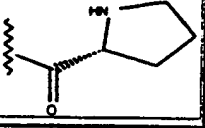
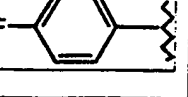
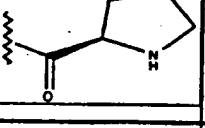
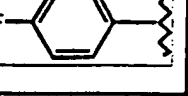
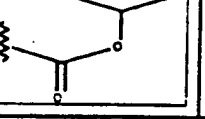
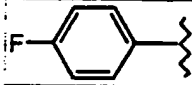
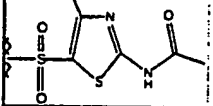
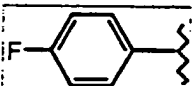
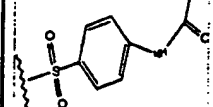
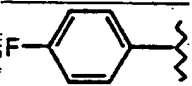
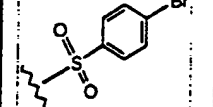
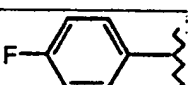
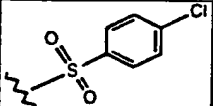
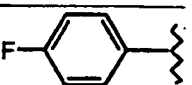
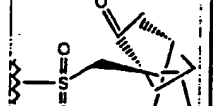
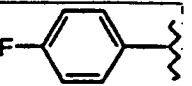
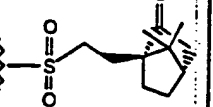
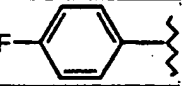
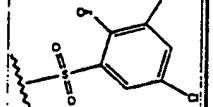
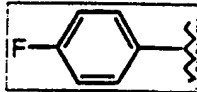
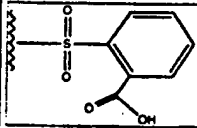
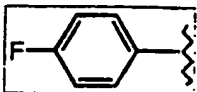
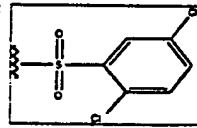
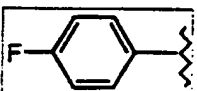
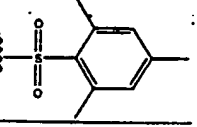
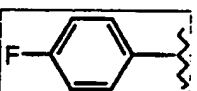
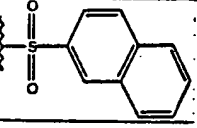
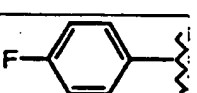
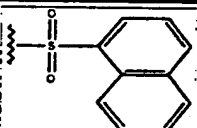
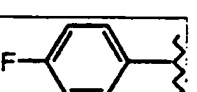
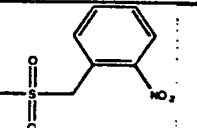
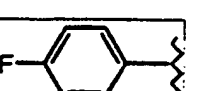
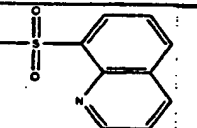
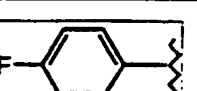
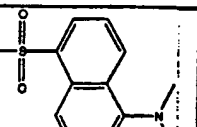
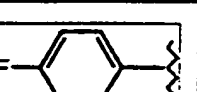
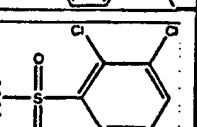
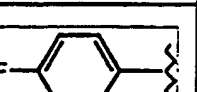
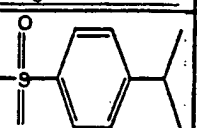


631

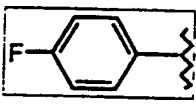
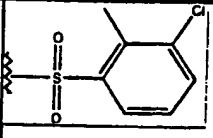
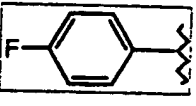
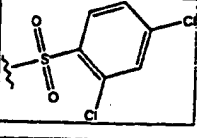
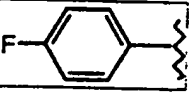
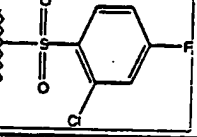
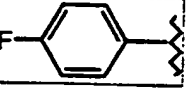
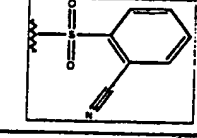
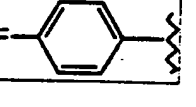
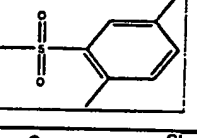
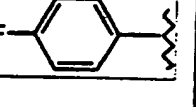
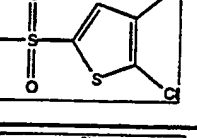
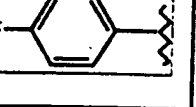
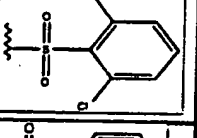
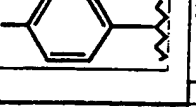
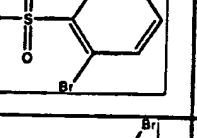
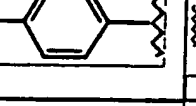
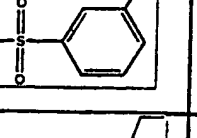
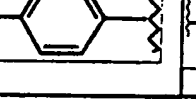
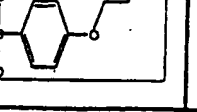
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0412			91	365	366
B-0413			79	367	368
B-0414			85	429	430
B-0415			82	401	402
B-0416			93	429	430
B-0417			97	429	430
B-0418			100	419	420
B-0419			100	431	432
B-0420			36	381	382
B-0421			96	353	354

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0422			100	461	462
B-0423			100	406	407
B-0424			76	366	367
B-0425			21	368	369
B-0426			100	354	355
B-0427			100	379	380
B-0428			100	379	380
B-0429			86	368	369

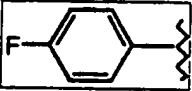
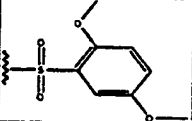
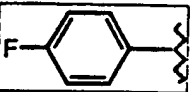
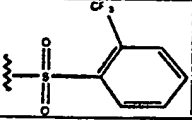
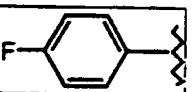
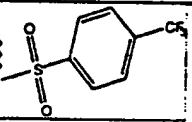
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0430			51	500	501
B-0431			76	479	480
B-0432			90	500	501
B-0433			96	456	457
B-0434			75	496	497
B-0435			52	496	497
B-0436			73	506	

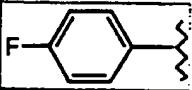
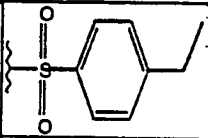
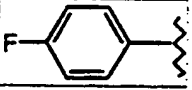
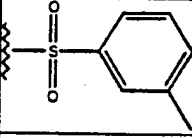
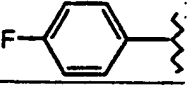
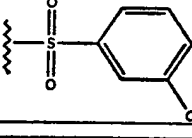
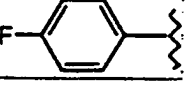
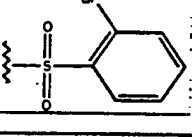
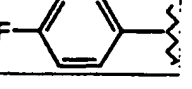
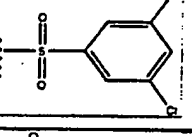
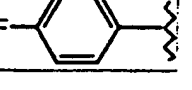
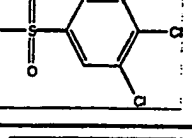
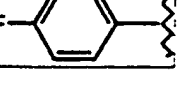
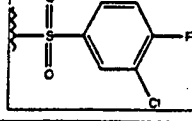
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0437			19	466	
B-0438			100	490	491
B-0439			67	464	465
B-0440			96	472	473
B-0441			87	472	473
B-0442			72	481	482
B-0443			66	473	474
B-0444			80	515	516
B-0445			94	490	491
B-0446			84	464	465

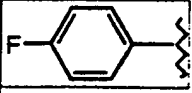
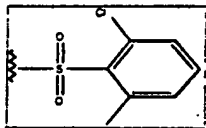
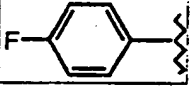
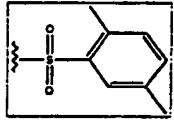
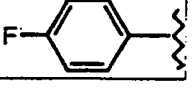
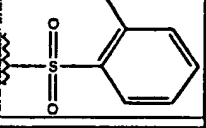
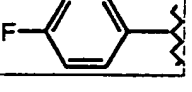
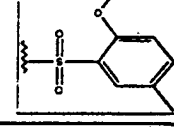
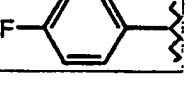
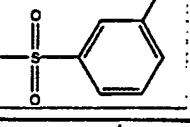
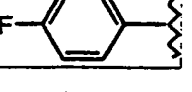
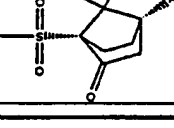
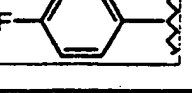
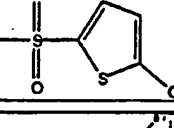
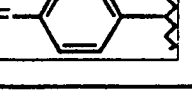
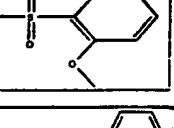
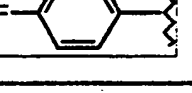
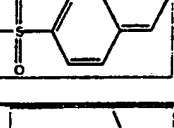
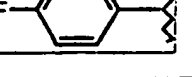
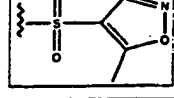


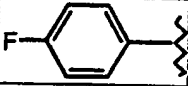
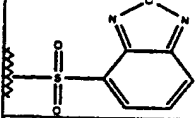
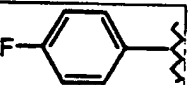
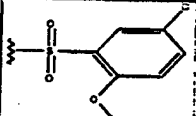
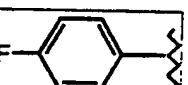
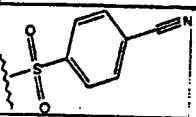
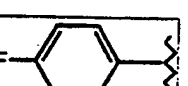
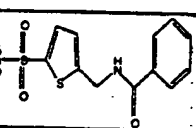
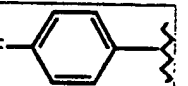
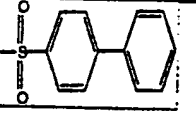
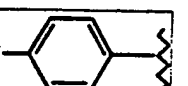
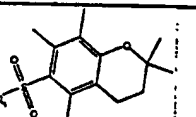
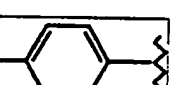
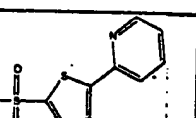
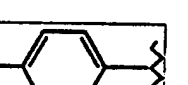
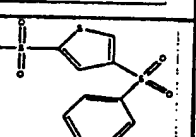
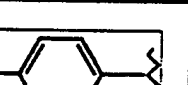
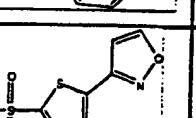

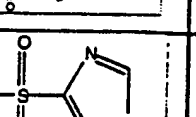
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0447			89	470	471
B-0448			100	490	491
B-0449			100	474	475
B-0450			100	447	448
B-0451			100	454	455
B-0452			95	496	497
B-0453			100	490	491
B-0454			100	500	501
B-0455			96	500	501
B-0456			89	494	495

636

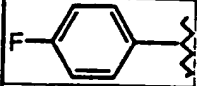
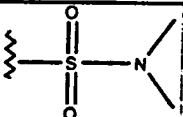
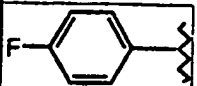
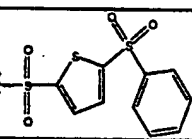
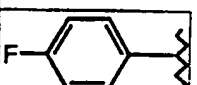
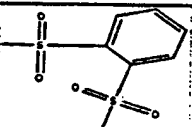
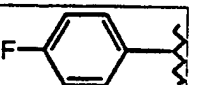
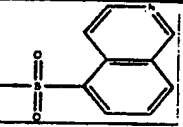
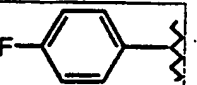
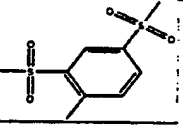
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0457			93	482	483
B-0458			100	490	491
B-0459			100	490	491


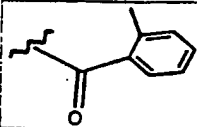
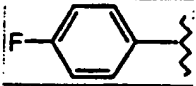
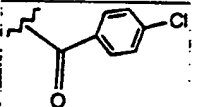
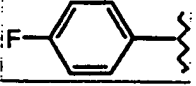
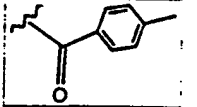
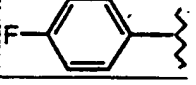
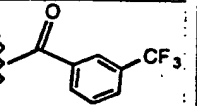
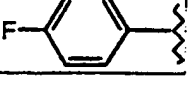
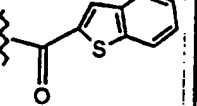
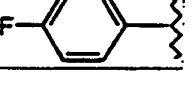
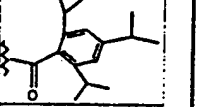
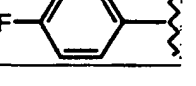
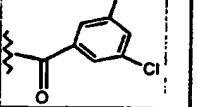
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0460			93	450	451
B-0461			84	452	453
B-0462			96	456	457
B-0463			66	456	457
B-0464			69	490	491
B-0465			86	490	491
B-0466			78	474	475

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0467			78	470	471
B-0468			91	450	451
B-0469			85	436	437
B-0470			99	466	467
B-0471			100	490	491
B-0472			37	482	483
B-0473			92	462	463
B-0474			99	530	532
B-0475			55	472	473
B-0476			89	441	442

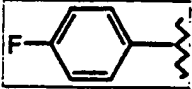
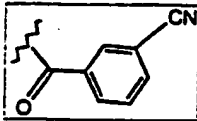
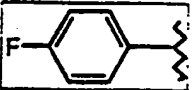
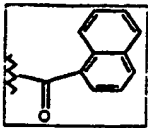
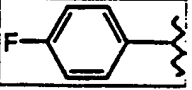
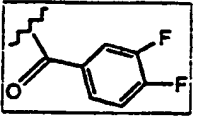
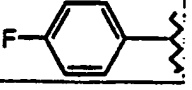
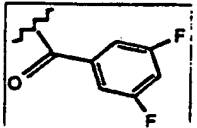
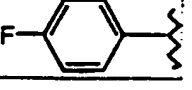
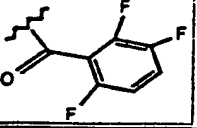
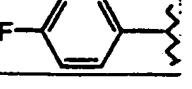
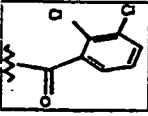
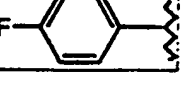
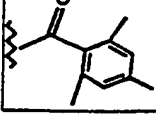
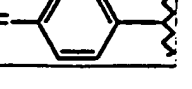
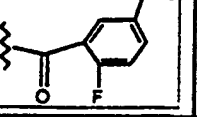
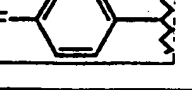
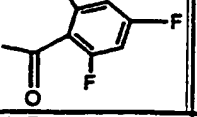
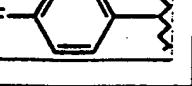
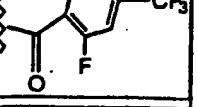
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0477			79	464	465
B-0478			92	486	487
B-0479			97	447	448
B-0480			75	561	562
B-0481			74	498	499
B-0482			57	548	549
B-0483			83	505	506
B-0484			100	568	569
B-0485			100	495	496
B-0486			100	426	427

640

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0487			32	389	390
B-0488			100	568	569
B-0489			91	500	501
B-0490			40	473	474
B-0491			73	514	515

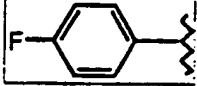
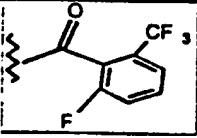
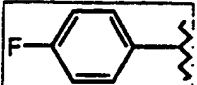
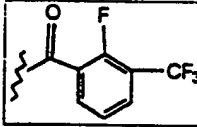
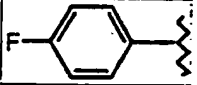
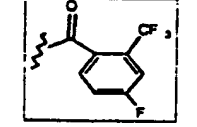
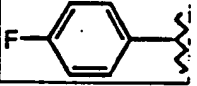
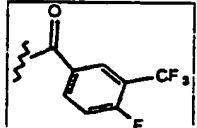
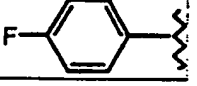
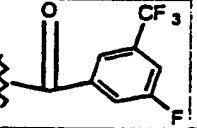
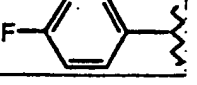
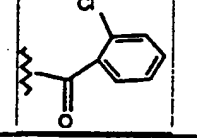
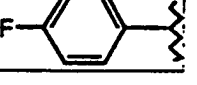
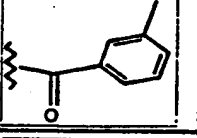
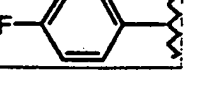
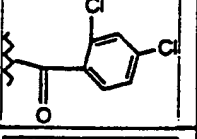
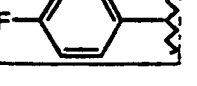
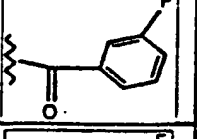
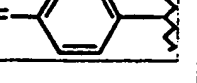
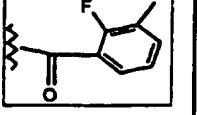
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0492			89	400	401
B-0493			100	420	421
B-0494			100	400	401
B-0495			100	454	455
B-0496			100	442	443
B-0497			50	512	513
B-0498			100	454	455

642

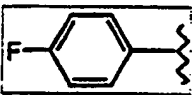
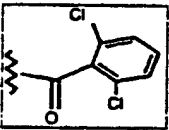
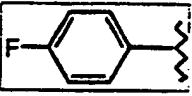
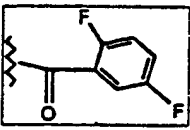
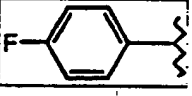
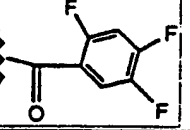
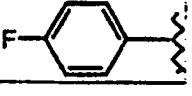
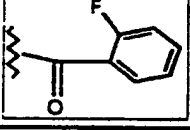
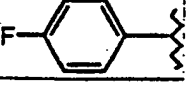
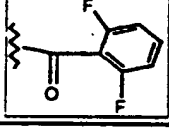
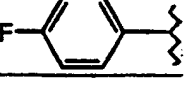
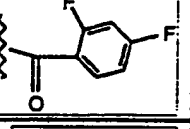
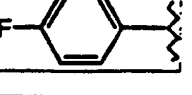
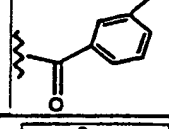
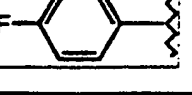
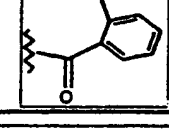
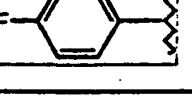
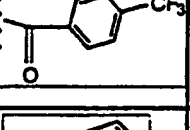
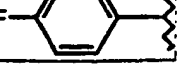
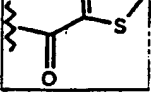
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0499			98	411	412
B-0500			100	436	437
B-0501			100	422	423
B-0502			100	422	423
B-0503			92	440	441
B-0504			67	454	455
B-0505			68	428	429
B-0506			98	472	473
B-0507			82	440	441
B-0508			99	472	473



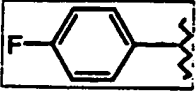
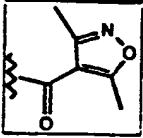
643

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0509			100	472	473
B-0510			96	472	473
B-0511			100	472	473
B-0512			100	472	473
B-0513			100	472	473
B-0514			100	420	421
B-0515			100	400	401
B-0516			100	454	455
B-0517			100	404	405
B-0518			99	422	423

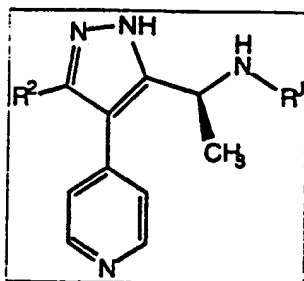
644

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0519			100	454	455
B-0520			98	422	423
B-0521			99	440	441
B-0522			88	404	405
B-0523			100	422	423
B-0524			100	422	423
B-0525			100	420	421
B-0526			100	464	465
B-0527			100	454	455
B-0528			100	392	393

645

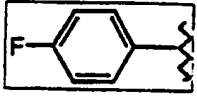
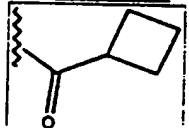
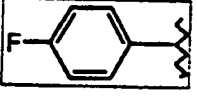
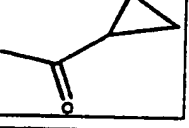
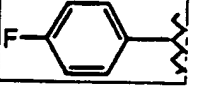
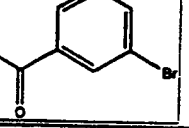
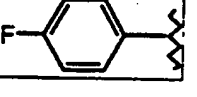
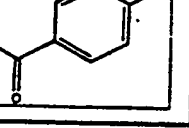
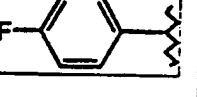
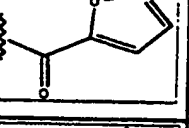
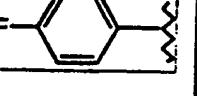

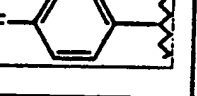


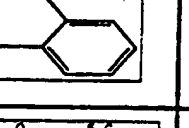
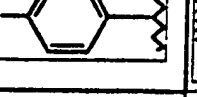
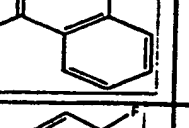
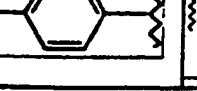
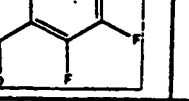
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0529			94	405	406

646

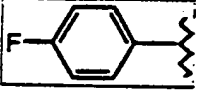
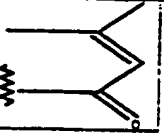
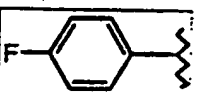
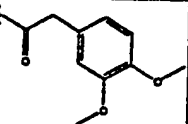
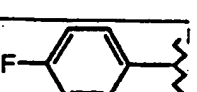
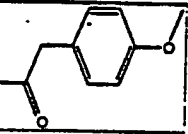
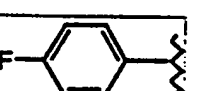
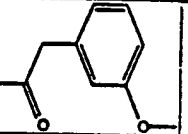
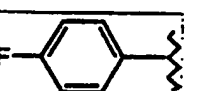
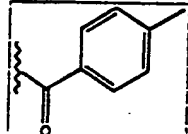
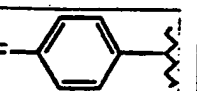
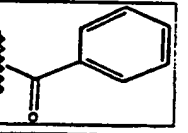
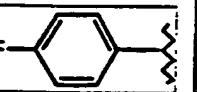
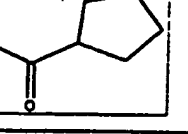
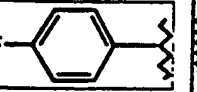
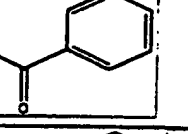
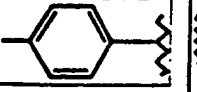
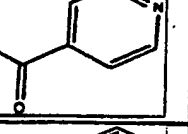
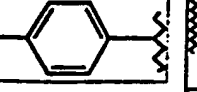
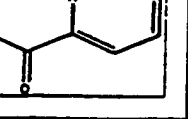


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0530			67	382	383
B-0531			66	512	513
B-0532			37	352	353
B-0533			56	404	405
B-0534			100	366	367
B-0535			100	410	411
B-0536			41	324	325

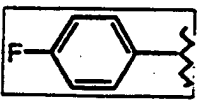
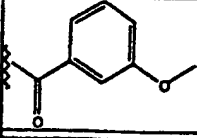
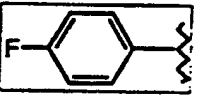
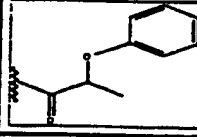
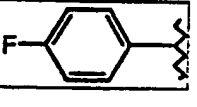
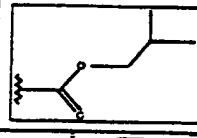
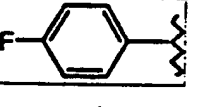
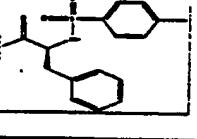
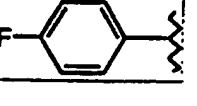
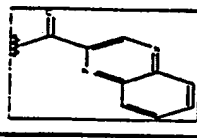
647

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0537			100	364	365
B-0538			29	350	351
B-0539			70	464	465
B-0540			50	512	513
B-0541			61	377	378
B-0542			61	396	397
B-0543			59	354	355
B-0544			45	416	417
B-0545			100	454	455
B-0546			44	440	441

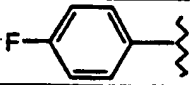
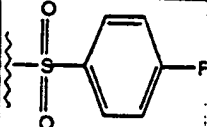
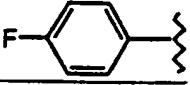
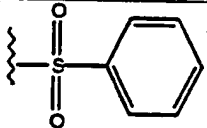
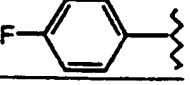
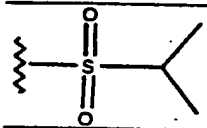
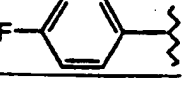
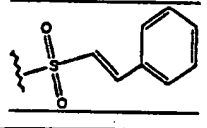
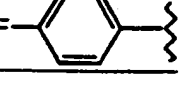

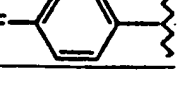
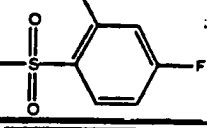
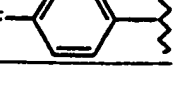
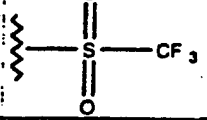
648

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0547			64	364	365
B-0548			89	460	461
B-0549			100	430	431
B-0550			100	430	431
B-0551			81	400	401
B-0552			38	386	387
B-0553			31	378	379
B-0554			100	387	388
B-0555			66	387	388
B-0556			32	387	388

649

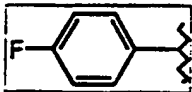
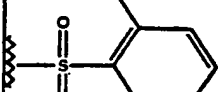
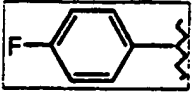
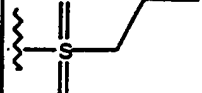
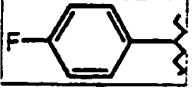

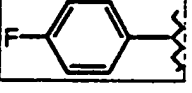

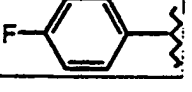
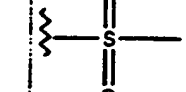
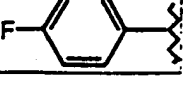
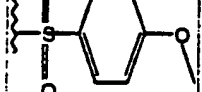
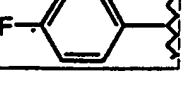
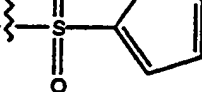
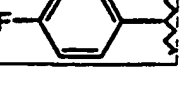
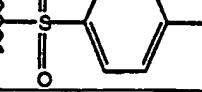
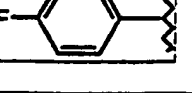
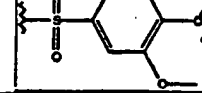
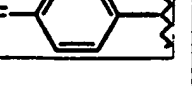
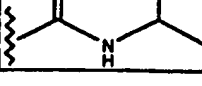
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0557			70	416	417
B-0558			57	430	431
B-0559			74	382	383
B-0560			36	583	584
B-0561			51	438	439

650

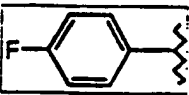
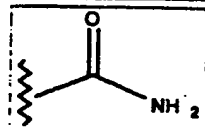
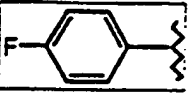
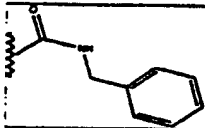
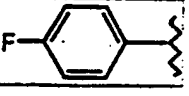
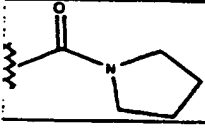
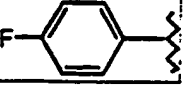
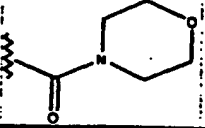
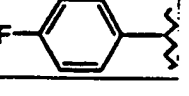
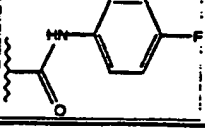
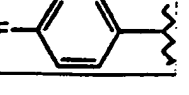
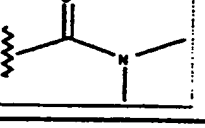
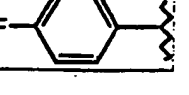
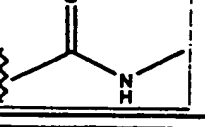
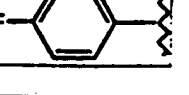
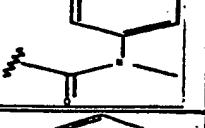
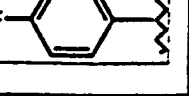
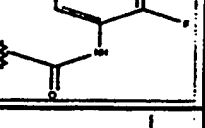
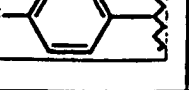
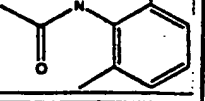
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0562			88	440	441
B-0563			68	422	423
B-0564			47	388	389
B-0565			100	448	449
B-0566			76	436	437
B-0567			99	458	459
B-0568			45	414	415



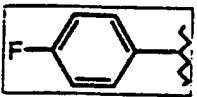
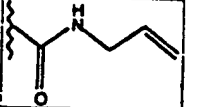
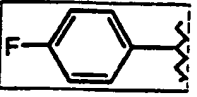
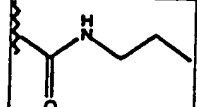
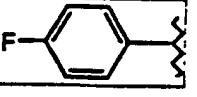
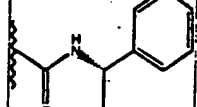
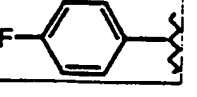
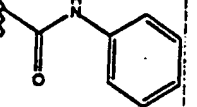
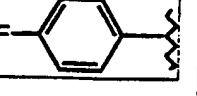

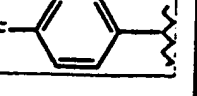
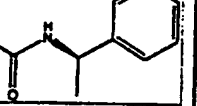
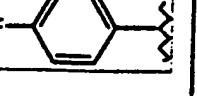
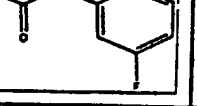
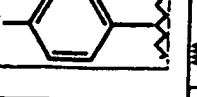

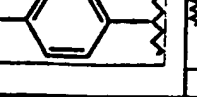
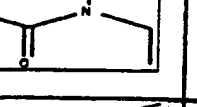
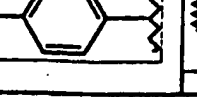
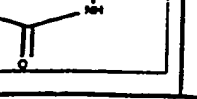
651

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0569			88	440	441
B-0570			61	388	389
B-0571			58	402	403
B-0572			75	374	375
B-0573			72	360	361
B-0574			97	452	453
B-0575			71	428	429
B-0576			88	436	437
B-0577			72	482	483
B-0578			89	367	368

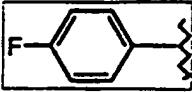
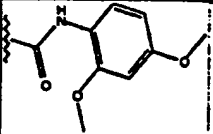
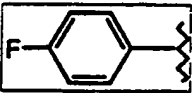
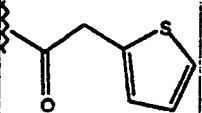
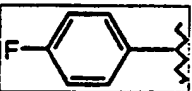
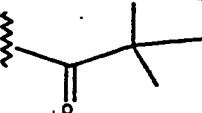
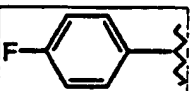

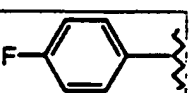
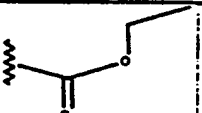
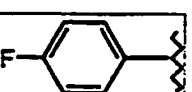

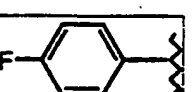
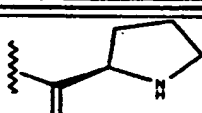
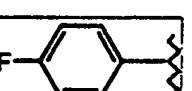
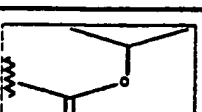
652

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0579			100	325	326
B-0580			75	415	416
B-0581			44	379	380
B-0582			75	395	396
B-0583			80	419	420
B-0584			57	353	354
B-0585			83	339	340
B-0586			71	415	416
B-0587			100	419	420
B-0588			94	429	430

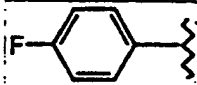
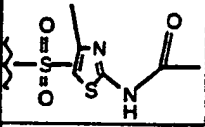
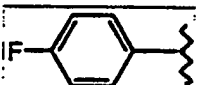
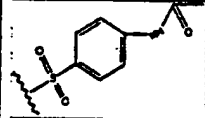
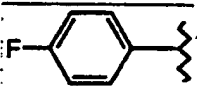
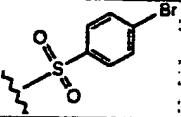
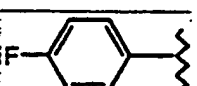
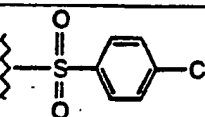
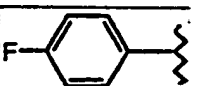
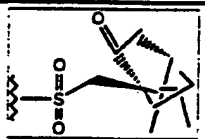
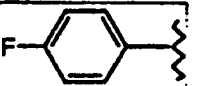
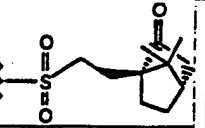
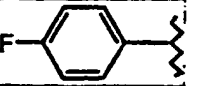
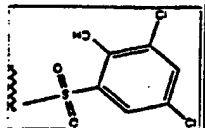
653

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0589			78	365	366
B-0590			82	367	368
B-0591			72	429	430
B-0592			82	401	402
B-0593			88	429	430
B-0594			100	429	430
B-0595			99	419	420
B-0596			93	431	432
B-0597			40	381	382
B-0598			93	353	354

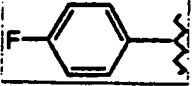
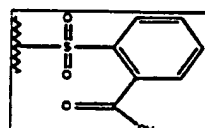
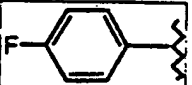
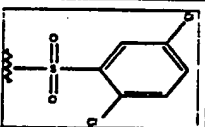
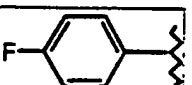
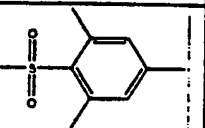
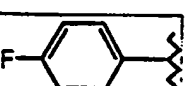
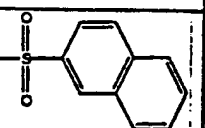
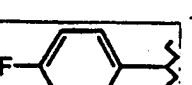
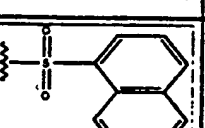

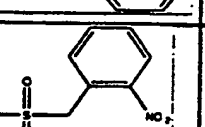
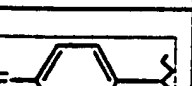
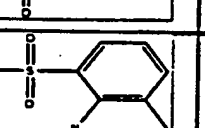

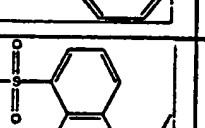

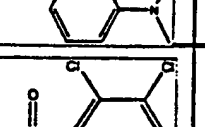

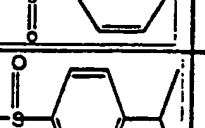
654

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0599			100	461	462
B-0600			98	406	407
B-0601			66	366	367
B-0602			25	368	369
B-0603			90	354	355
B-0604			86	379	380
B-0605			87	379	380
B-0606			72	368	369

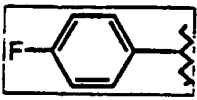
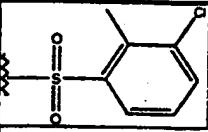
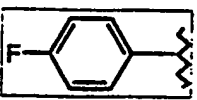
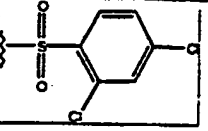
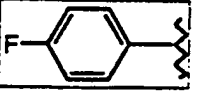
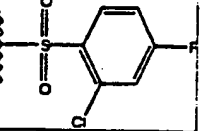
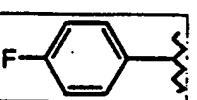
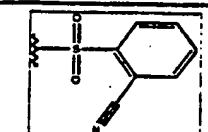
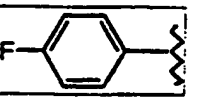
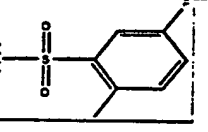
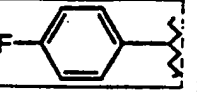
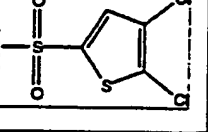
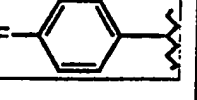
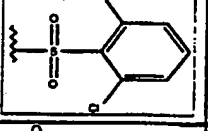
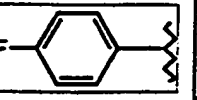
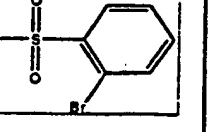
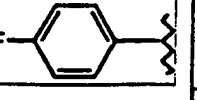
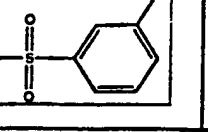
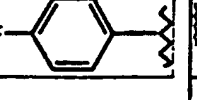
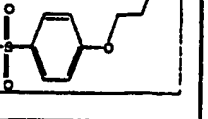
655

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0607			34	500	501
B-0608			100	479	480
B-0609			82	500	501
B-0610			100	456	457
B-0611			76	496	497
B-0612			69	496	497
B-0613			61	506	

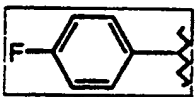
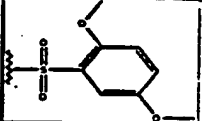
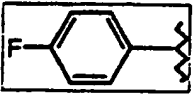
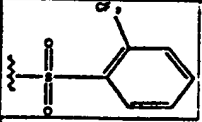
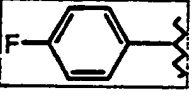
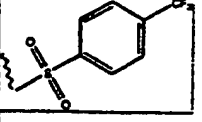
656

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0614			18	466	
B-0615			100	490	491
B-0616			77	464	465
B-0617			93	472	473
B-0618			84	472	473
B-0619			71	481	482
B-0620			89	473	474
B-0621			68	515	516
B-0622			70	490	491
B-0623			92	464	465

657

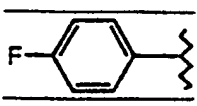
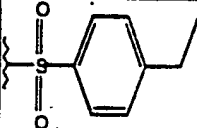
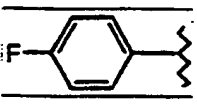
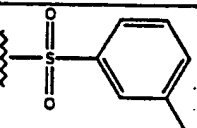
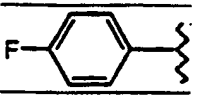
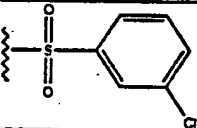
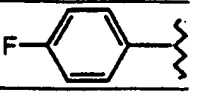
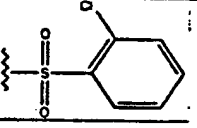
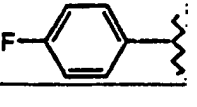
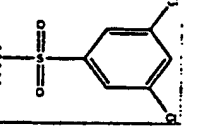
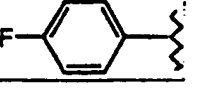
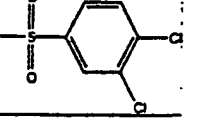
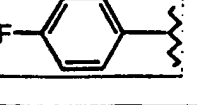
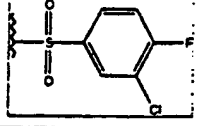
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0624			98	470	471
B-0625			96	490	491
B-0626			100	474	475
B-0627			100	447	448
B-0628			64	454	455
B-0629			100	496	497
B-0630			85	490	491
B-0631			75	500	501
B-0632			83	500	501
B-0633			58	494	495

658

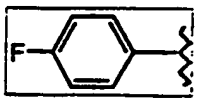
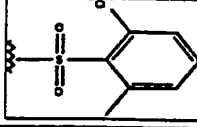
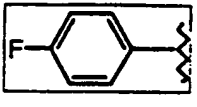
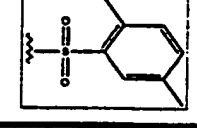
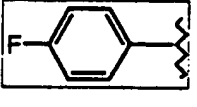
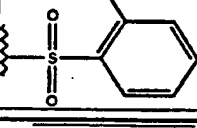
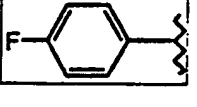
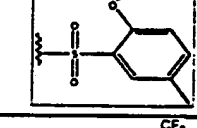
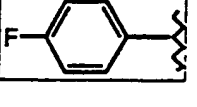
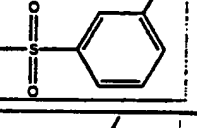
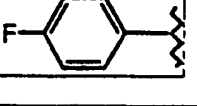
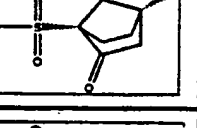
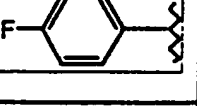
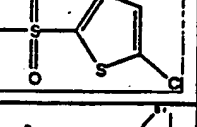
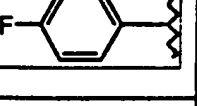
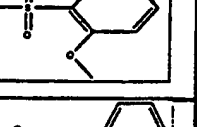
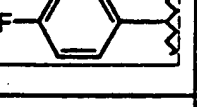
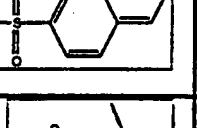
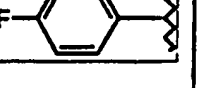
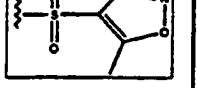
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0634			63	482	483
B-0635			95	490	491
B-0636			100	490	491




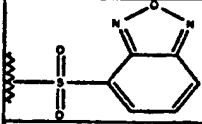
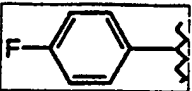
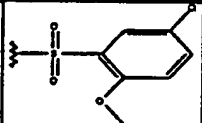
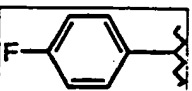
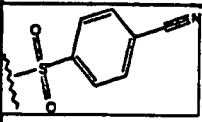
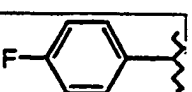
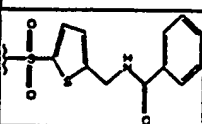
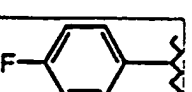
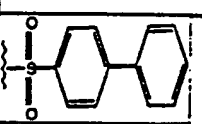
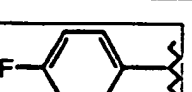
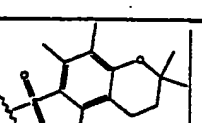
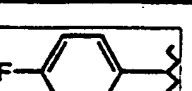
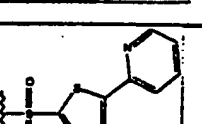
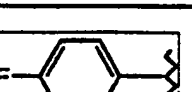
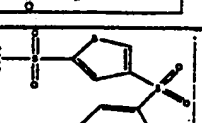
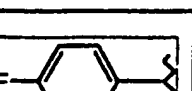
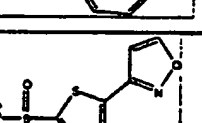

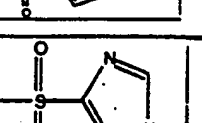
659

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0637			91	450	451
B-0638			96	436	437
B-0639			100	456	457
B-0640			100	456	457
B-0641			88	490	491
B-0642			99	490	491
B-0643			92	474	475

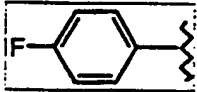
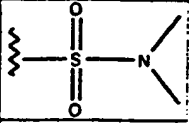
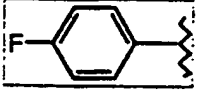
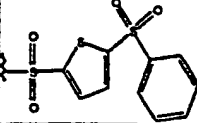
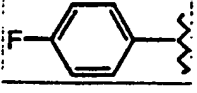

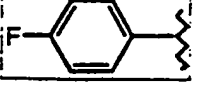
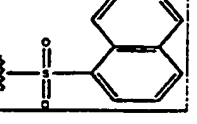
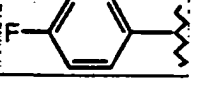
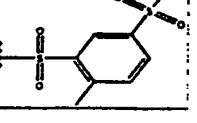
660

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0644			100	470	471
B-0645			92	450	451
B-0646			100	436	437
B-0647			90	466	467
B-0648			94	490	491
B-0649			57	482	
B-0650			82	462	463
B-0651			100	530	531
B-0652			53	472	
B-0653			84	441	442

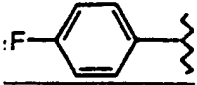
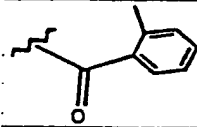
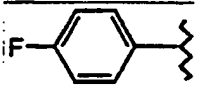
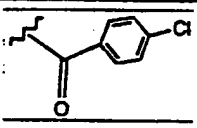
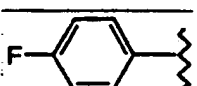
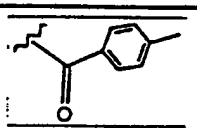
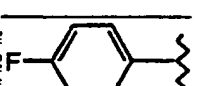
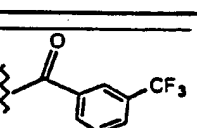
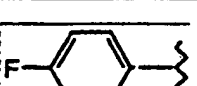
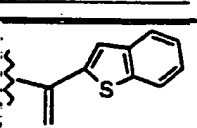
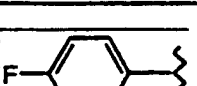
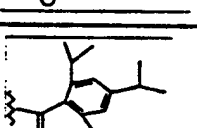

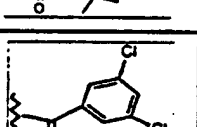
661

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0654			92	464	465
B-0655			100	486	487
B-0656			98	447	448
B-0657			85	561	562
B-0658			92	498	499
B-0659			46	548	549
B-0660			80	505	506
B-0661			100	568	569
B-0662			98	495	496
B-0663			74	426	427

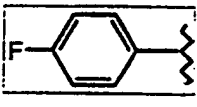
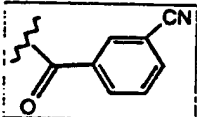
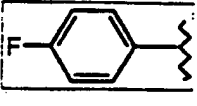
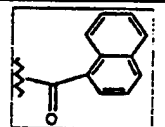
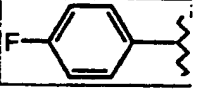
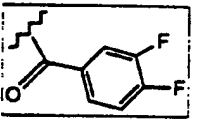
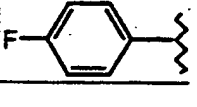
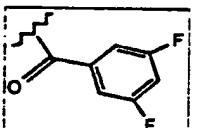
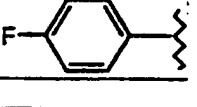
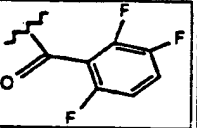
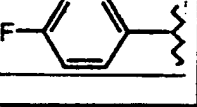
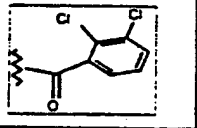
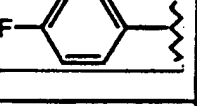
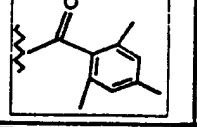
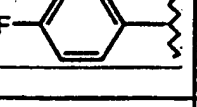
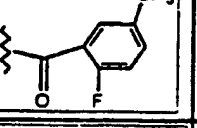
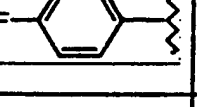
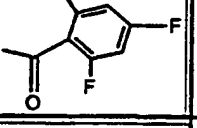
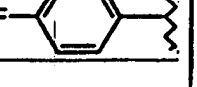
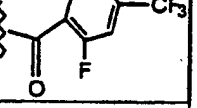
662

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0664			30	389	390
B-0665			100	568	569
B-0666			93	500	501
B-0667			54	473	474
B-0668			66	514	515

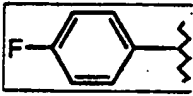
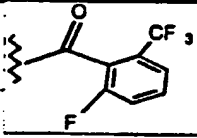
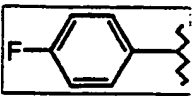
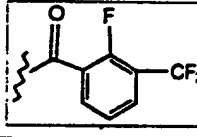
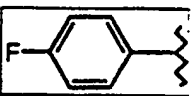
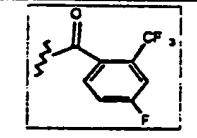
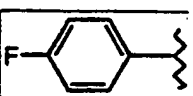
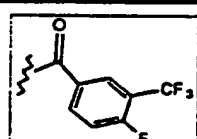
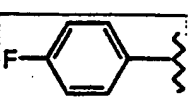
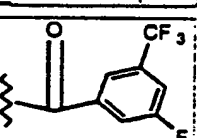
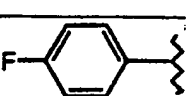
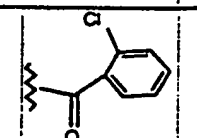
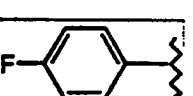
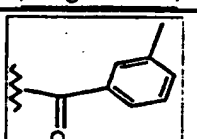
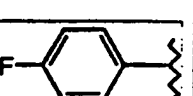
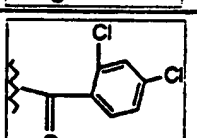
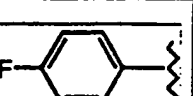
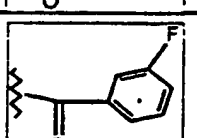
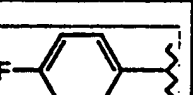
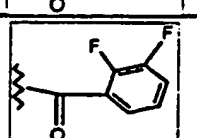
663

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0669			65	400	401
B-0670			45	420	421
B-0671			43	400	401
B-0672			45	454	455
B-0673			41	442	443
B-0674			16	512	513
B-0675			39	454	455

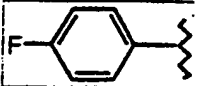
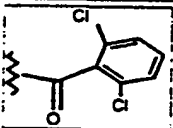
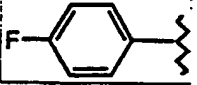
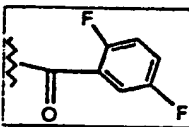
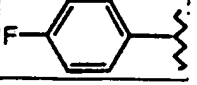
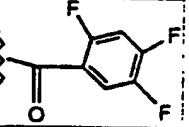
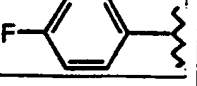
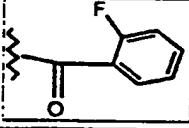
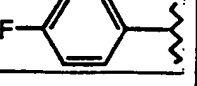
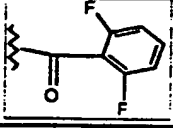
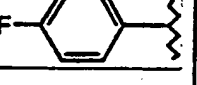
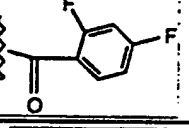
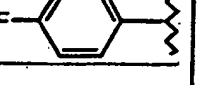
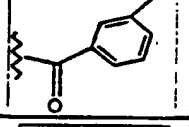
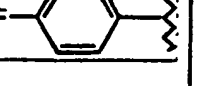
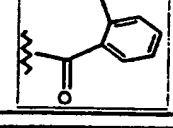
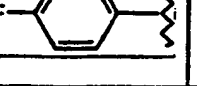
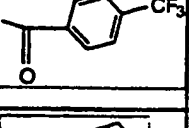
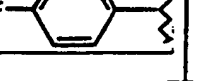
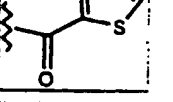
664

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0676			34	411	412
B-0677			46	436	437
B-0678			37	422	423
B-0679			34	422	423
B-0680			60	440	441
B-0681			31	454	455
B-0682			37	428	429
B-0683			46	472	473
B-0684			50	440	441
B-0685			44	472	473

665

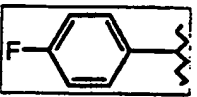
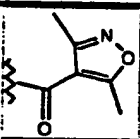
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0686			66	472	473
B-0687			57	472	473
B-0688			52	472	473
B-0689			42	472	473
B-0690			34	472	473
B-0691			52	420	421
B-0692			41	400	401
B-0693			56	454	455
B-0694			38	404	405
B-0695			43	422	423

666

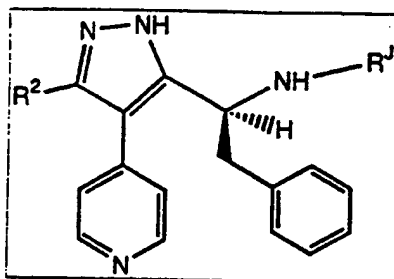
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0696			57	454	455
B-0697			51	422	423
B-0698			59	440	441
B-0699			46	404	405
B-0700			47	422	423
B-0701			46	422	423
B-0702			43	420	421
B-0703			57	464	465
B-0704			44	454	455
B-0705			33	392	393



667

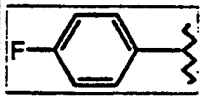
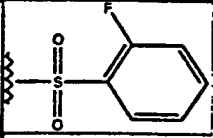
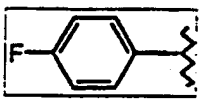
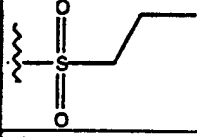
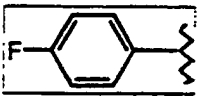
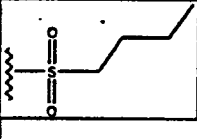
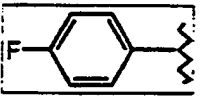
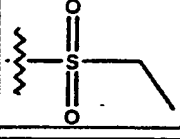
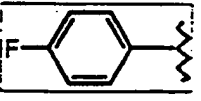
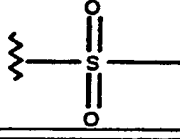
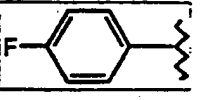
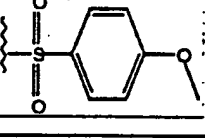
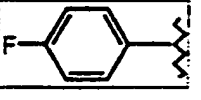
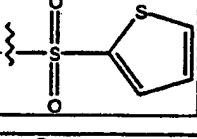
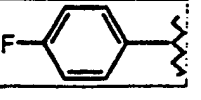
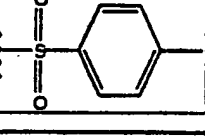
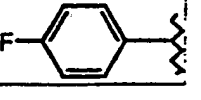
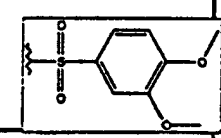
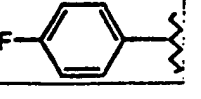
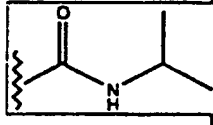
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0706			35	405	406

668

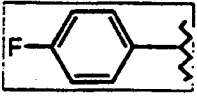
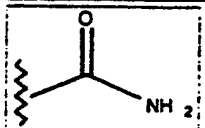
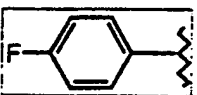
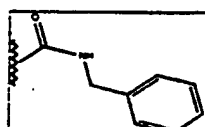
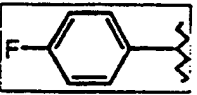
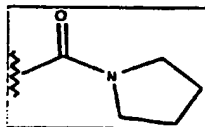
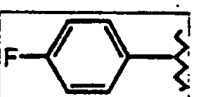
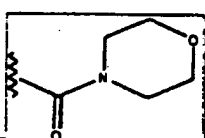
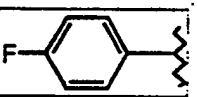
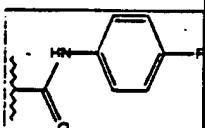
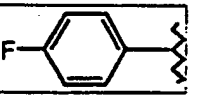
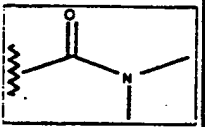
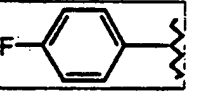
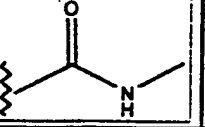
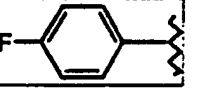
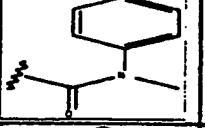
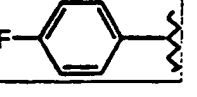
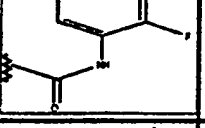
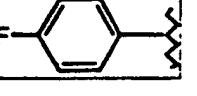
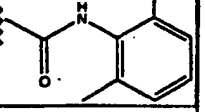


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0707			76	516	517
B-0708			61	498	499
B-0709			37	464	465
B-0710			76	524	525
B-0711			75	512	513
B-0712			91	534	535
B-0713			42	490	491

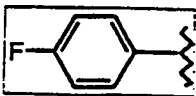
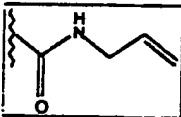
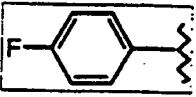
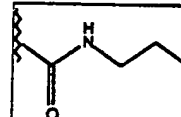
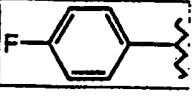
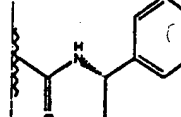
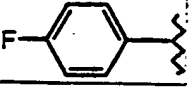
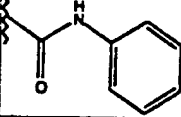
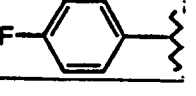

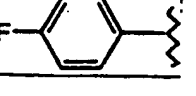
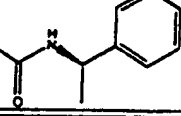
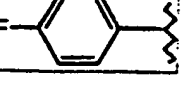
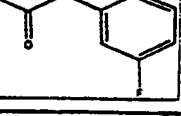
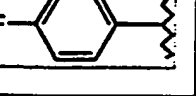

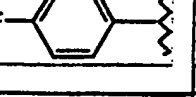

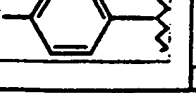

669

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0714			87	516	517
B-0715			60	464	465
B-0716			59	478	479
B-0717			61	450	451
B-0718			65	436	437
B-0719			84	528	529
B-0720			69	504	505
B-0721			63	512	513
B-0722			88	558	559
B-0723			68	443	444

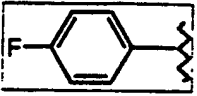
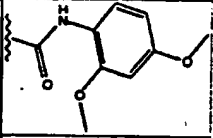
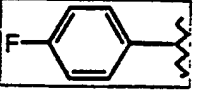
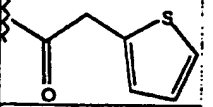
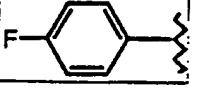
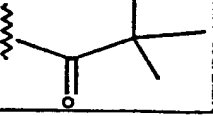
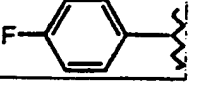
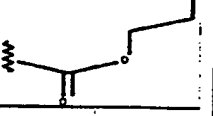
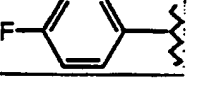
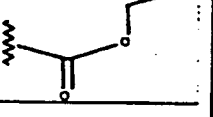
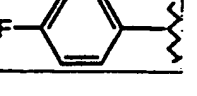
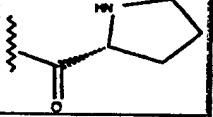
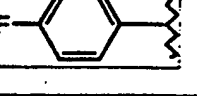
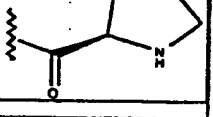
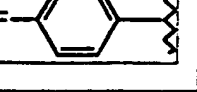
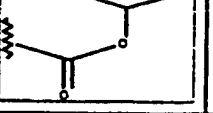
670

Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0724			75	401	402
B-0725			83	491	492
B-0726			24	455	456
B-0727			67	471	472
B-0728			89	495	496
B-0729			38	429	430
B-0730			76	415	416
B-0731			60	491	492
B-0732			86	495	496
B-0733			81	505	506

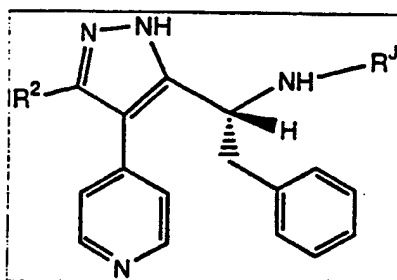
671

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0734			87	441	442
B-0735			83	443	444
B-0736			91	505	506
B-0737			9	477	-
B-0738			87	505	506
B-0739			82	505	506
B-0740			85	495	496
B-0741			68	507	508
B-0742			14	457	-
B-0743			77	429	430

672

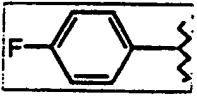
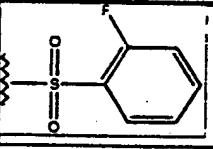
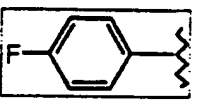
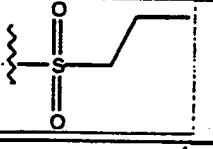
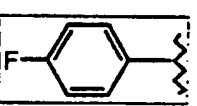
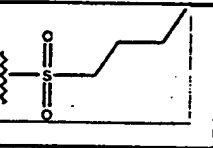
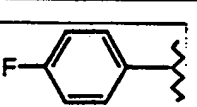
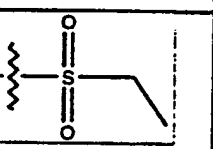
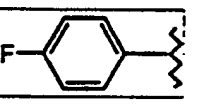
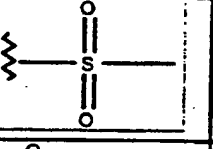
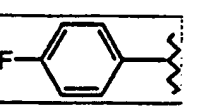
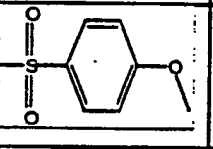
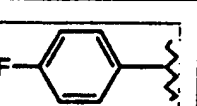
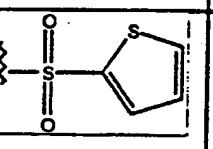
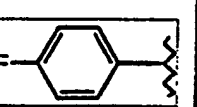
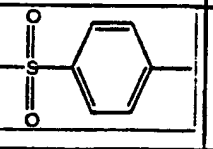
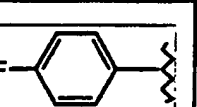
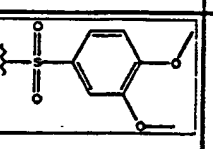
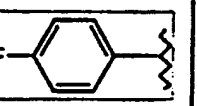
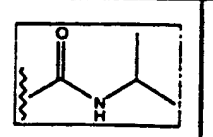
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0744			86	537	538
B-0745			82	482	483
B-0746			74	442	443
B-0747			83	444	445
B-0748			94	430	431
B-0749			100	455	456
B-0750			100	455	456
B-0751			48	444	445

673



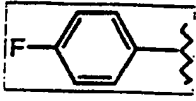
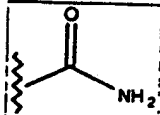
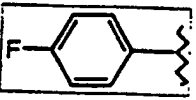
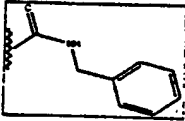
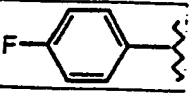
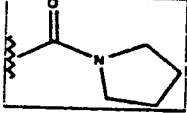
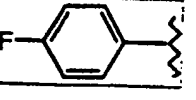
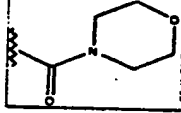
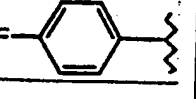
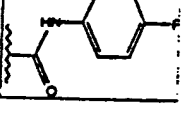
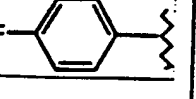
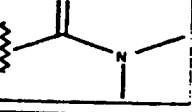
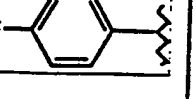
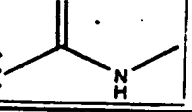
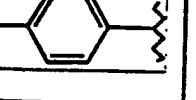

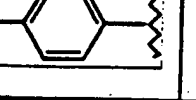
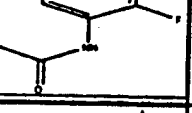
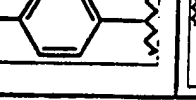
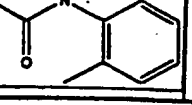
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0752			84	516	517
B-0753			67	498	499
B-0754			31	464	465
B-0755			85	524	525
B-0756			77	512	513
B-0757			57	534	535
B-0758			36	490	491

674

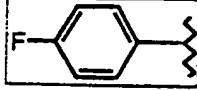
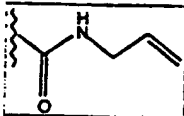
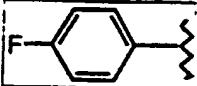
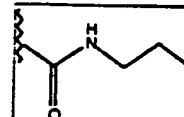
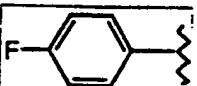
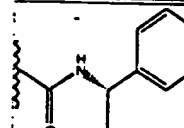
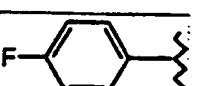
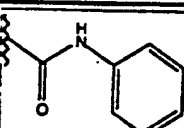
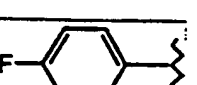


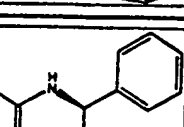

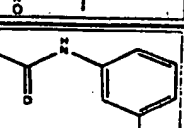

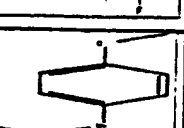


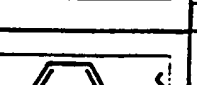

Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0759			79	516	517
B-0760			53	464	465
B-0761			50	478	479
B-0762			60	450	451
B-0763			75	436	437
B-0764			43	528	529
B-0765			75	504	505
B-0766			67	512	513
B-0767			43	558	559
B-0768			78	443	444



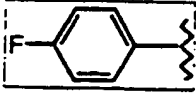
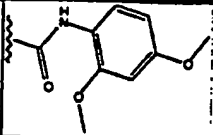
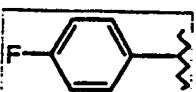
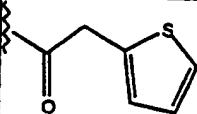
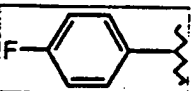
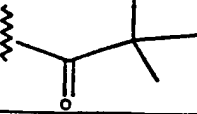
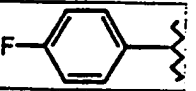
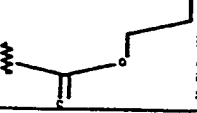
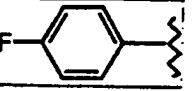
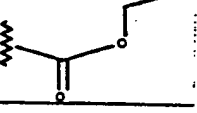
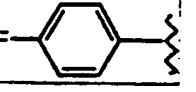
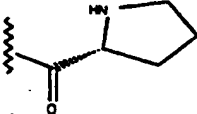
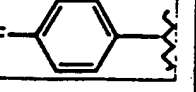
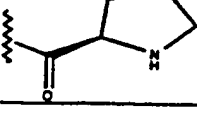
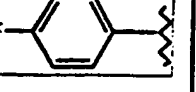
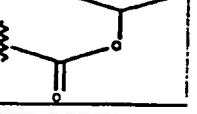
675

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0769			76	401	402
B-0770			57	491	492
B-0771			14	455	456
B-0772			72	471	472
B-0773			100	495	496
B-0774			41	429	430
B-0775			91	415	416
B-0776			64	491	492
B-0777			90	495	496
B-0778			19	505	506

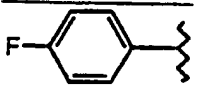
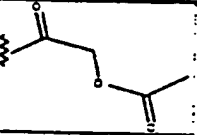
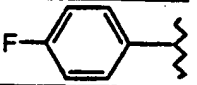
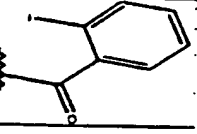
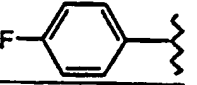
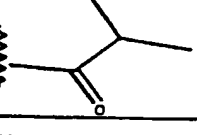
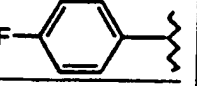
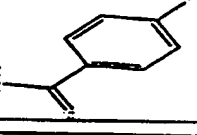
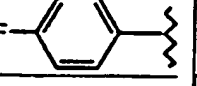
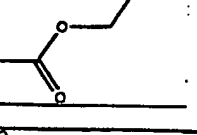
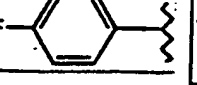
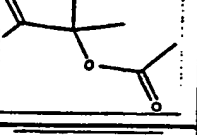
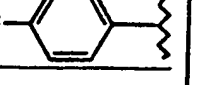
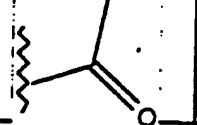
676

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0779			79	441	442
B-0780			40	443	444
B-0781			93	505	506
B-0782			57	477	478
B-0783			99	505	506
B-0784			100	505	506
B-0785			92	495	496
B-0786			91	507	508
B-0787			15	457	458
B-0788			48	429	430

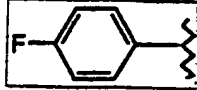
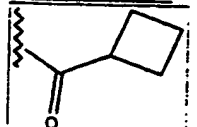
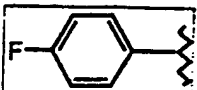
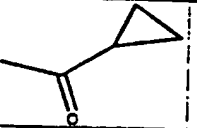
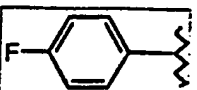
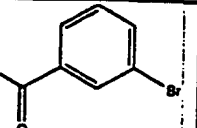
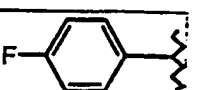
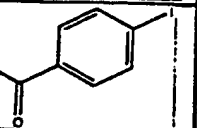
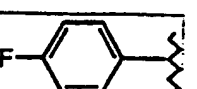
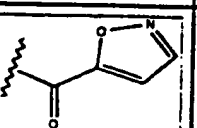
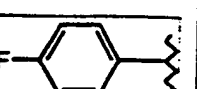
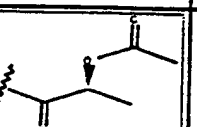
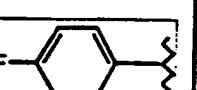
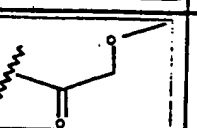
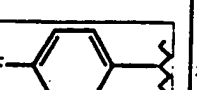
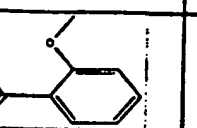
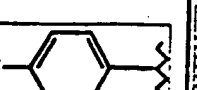
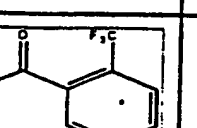
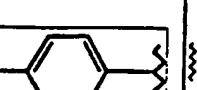
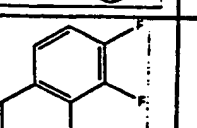
677

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0789			91	537	538
B-0790			93	482	483
B-0791			76	442	443
B-0792			96	444	445
B-0793			54	430	431
B-0794			100	455	456
B-0795			100	455	456
B-0796			94	444	445

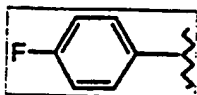
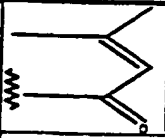
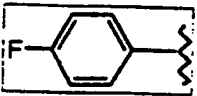
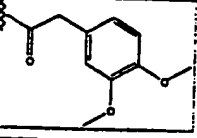
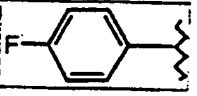
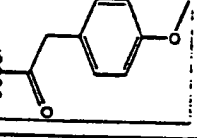
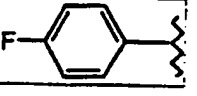
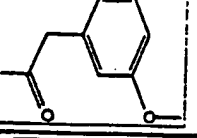
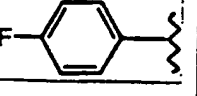
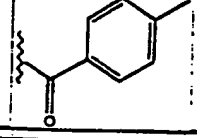
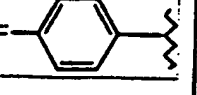
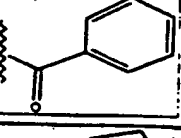
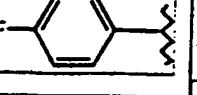
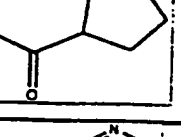
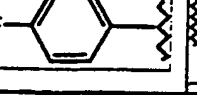
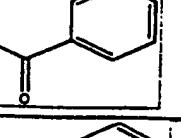
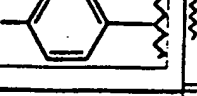
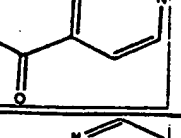
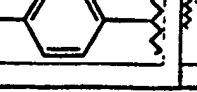
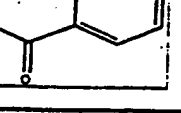
678

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0797			90	458	459
B-0798			90	588	589
B-0799			82	428	429
B-0800			92	480	481
B-0801			82	442	443
B-0802			95	486	487
B-0803			89	400	401

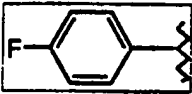
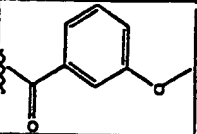
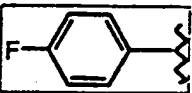
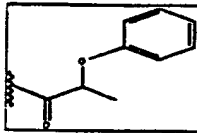
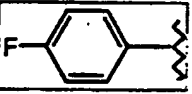
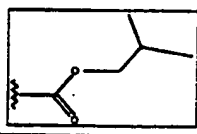
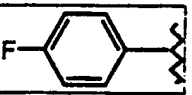
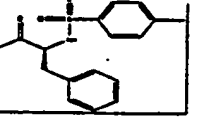
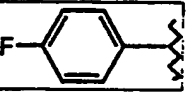
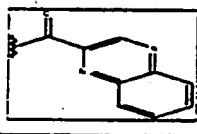
679

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0804			87	440	441
B-0805			100	426	427
B-0806			99	540	541
B-0807			96	588	589
B-0808			82	453	454
B-0809			92	472	473
B-0810			98	430	431
B-0811			88	492	493
B-0812			81	530	531
B-0813			98	516	517

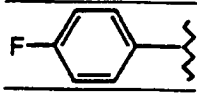
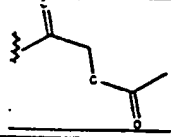
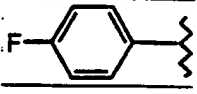
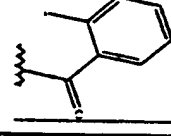
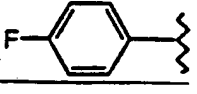
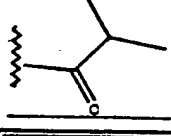
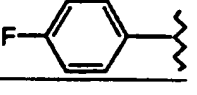
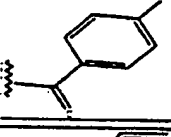
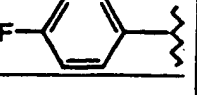
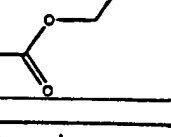
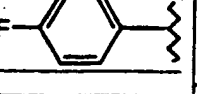
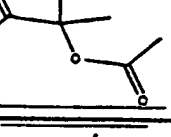
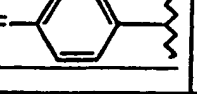
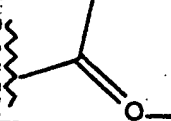
680

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0814			100	440	441
B-0815			100	536	537
B-0816			99	506	507
B-0817			98	506	507
B-0818			86	476	477
B-0819			90	462	463
B-0820			91	454	455
B-0821			69	463	464
B-0822			79	463	464
B-0823			79	463	464

681

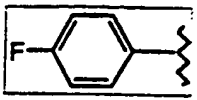
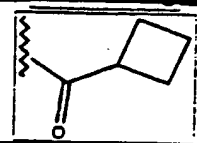
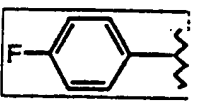
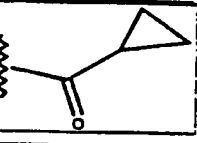
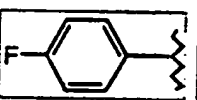
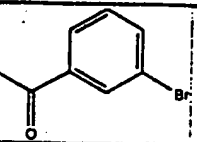
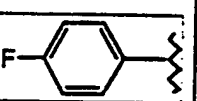
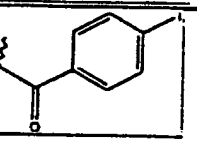
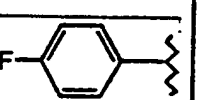
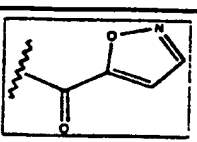
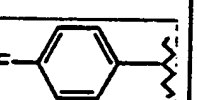
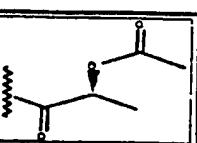
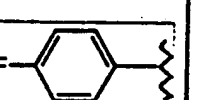
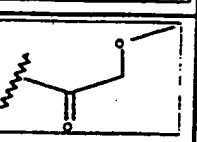
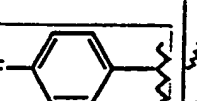
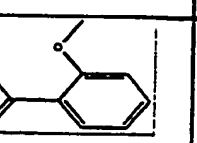
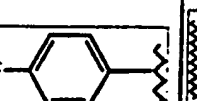
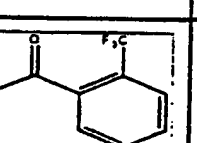
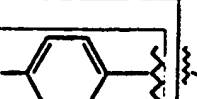
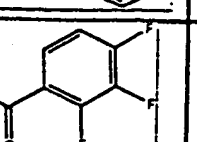
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0824			82	492	493
B-0825			100	506	507
B-0826			97	458	459
B-0827			100	659	660
B-0828			97	514	515

682

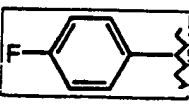
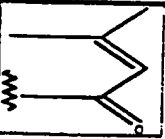
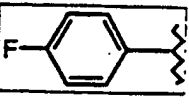
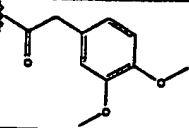
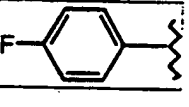
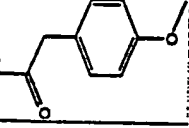
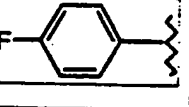
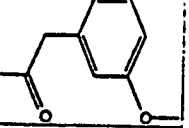
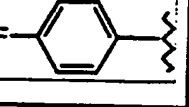
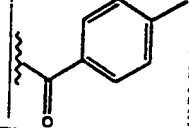
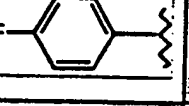
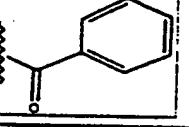
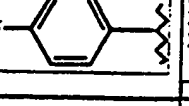
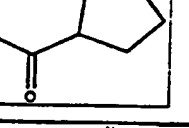
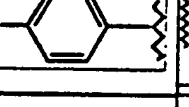
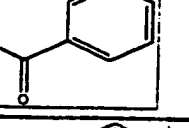
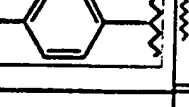
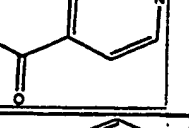
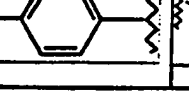
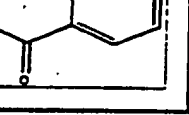
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0829			63	458	459
B-830			70	588	589
B-0831			100	428	429
B-0832			81	480	481
B-0833			73	442	443
B-0834			79	486	487
B-0835			5	400	401



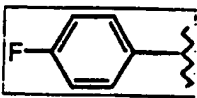
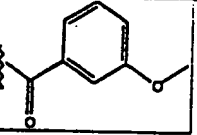
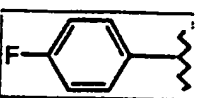
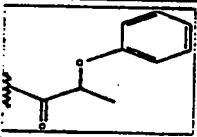
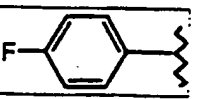
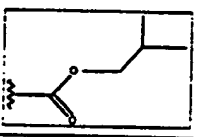
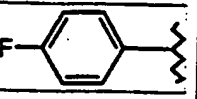
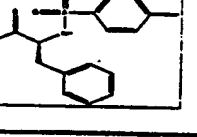

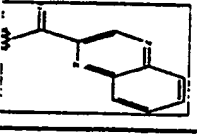
683

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0836			28	440	441
B-0837			81	426	427
B-0838			84	540	541
B-0839			80	588	589
B-0840			71	453	454
B-0841			55	472	473
B-0842			71	430	431
B-0843			68	492	493
B-0844			61	530	531
B-0845			84	516	517

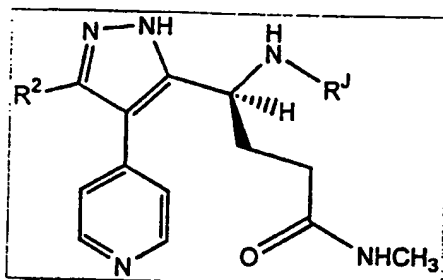
684

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0846			87	440	441
B-0847			86	536	537
B-0848			79	506	507
B-0849			81	506	507
B-0850			69	476	477
B-0851			83	462	463
B-0852			77	454	455
B-0853			87	463	464
B-0854			73	463	464
B-0855			92	463	464

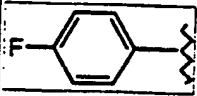
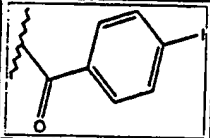
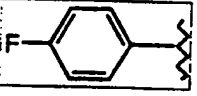
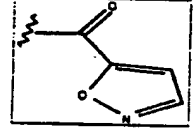
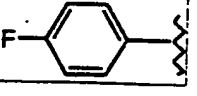
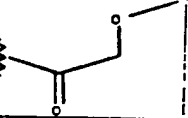
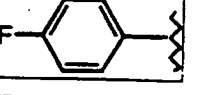
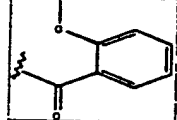
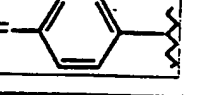
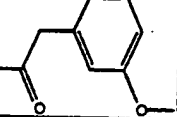
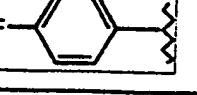
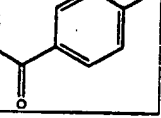
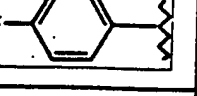
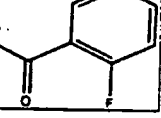
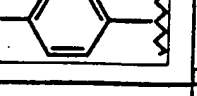
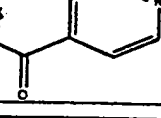
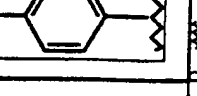
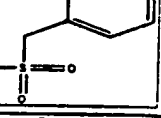
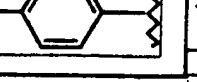
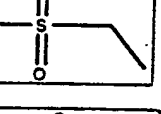
685

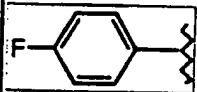
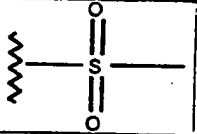
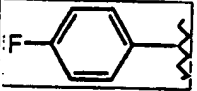
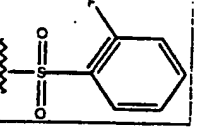
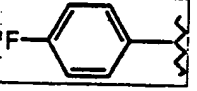
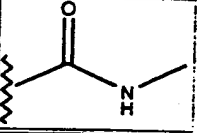
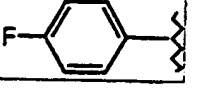
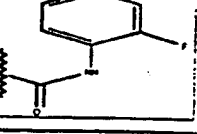
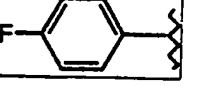
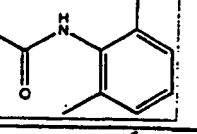
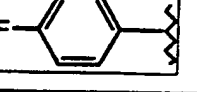
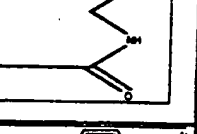
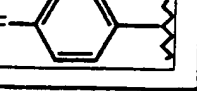
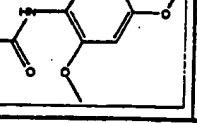
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0856			75	492	493
B-0857			86	506	507
B-0858			84	458	459
B-0859			80	659	660
B-0860			94	514	515

686

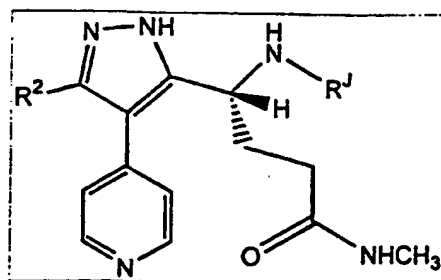


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0861			84	583	584
B-0862			96	475	476
B-0863			69	423	424
B-0864			86	437	438
B-0865			62	395	-
B-0866			81	421	422
B-0867			100	535	536

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0868			89	583	584
B-0869			100	448	449
B-0870			100	425	426
B-0871			100	487	488
B-0872			78	501	502
B-0873			78	471	472
B-0874			92	475	476
B-0875			37	458	459
B-0876			69	507	508
B-0877			70	445	446

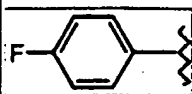
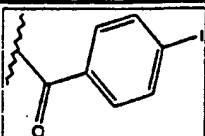
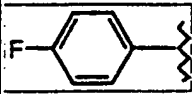
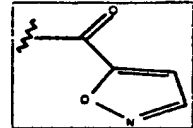
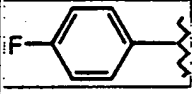
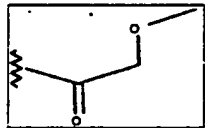
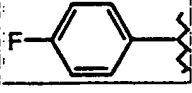
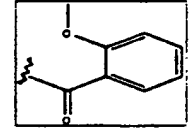
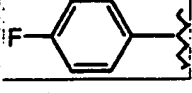
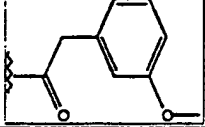
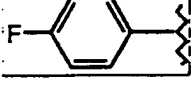
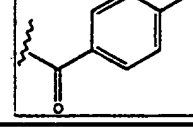
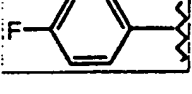
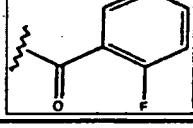
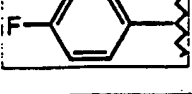
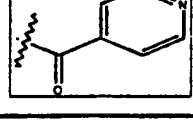
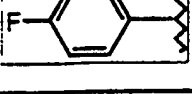
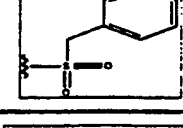

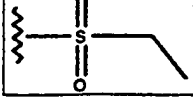
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0878			91	431	432
B-0879			92	511	512
B-0880			89	410	411
B-0881			84	490	491
B-0882			85	500	501
B-0883			85	424	425
B-0884			86	532	533

689



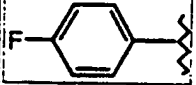
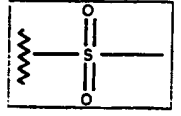
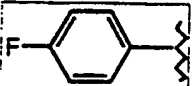
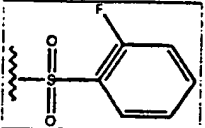
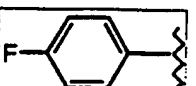
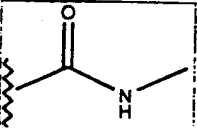
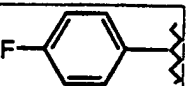
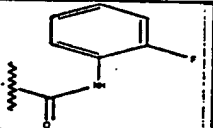
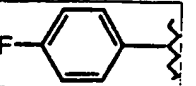
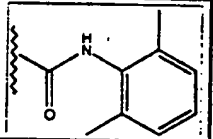
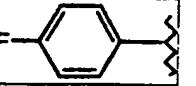
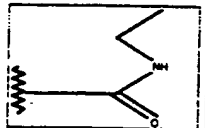
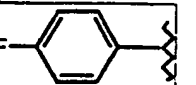
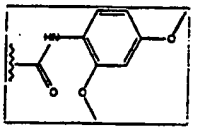
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0885			51	583	-
B-0886			97	475	-
B-0887			29	423	424
B-0888			82	437	438
B-0889			93	395	396
B-0890			91	421	422
B-0891			43	535	536

690

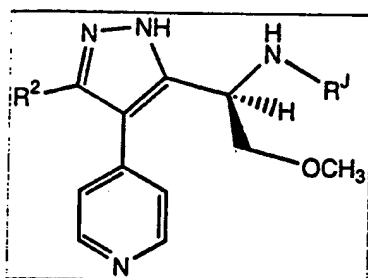
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0892			62	583	584
B-0893			95	448	449
B-0894			100	425	426
B-0895			76	487	488
B-0896			62	501	502
B-0897			80	471	472
B-0898			79	475	476
B-0899			70	458	459
B-0900			62	507	508
B-0901			43	445	446



691

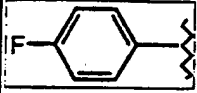
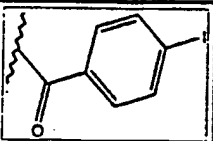
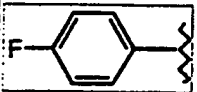
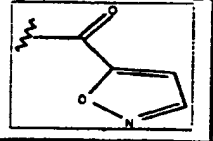
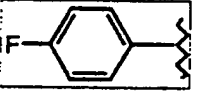
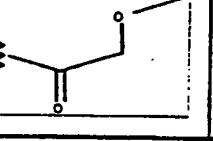
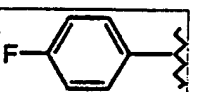
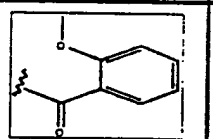
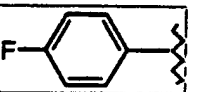
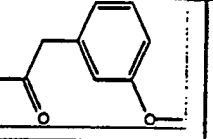
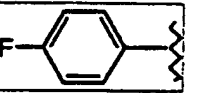
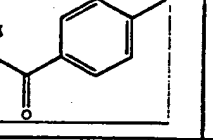
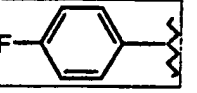
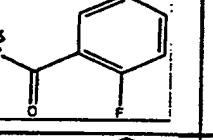
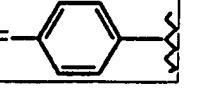
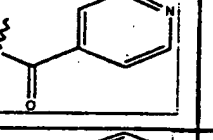
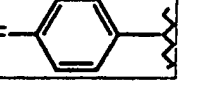

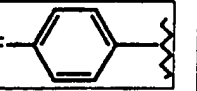
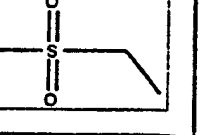
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0902			93	431	432
B-0903			100	511	512
B-0904			95	410	411
B-0905			89	490	491
B-0906			69	500	501
B-0907			28	424	425
B-0908			64	532	533

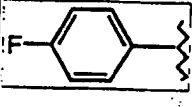
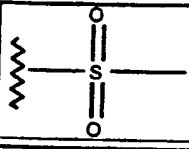
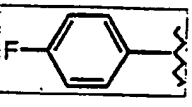
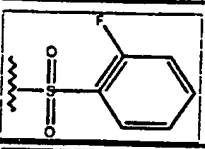
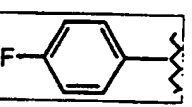
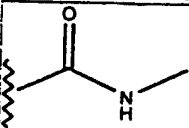
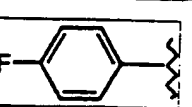
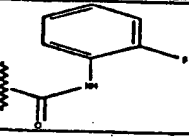
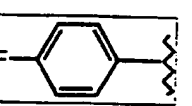
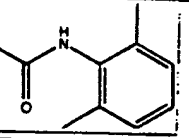
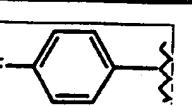
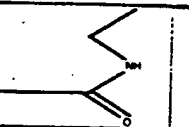
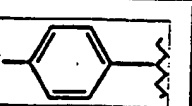
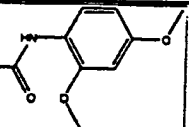
692

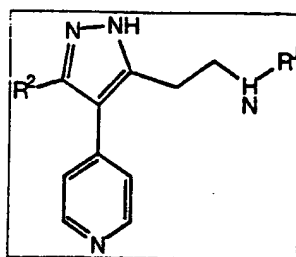


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0909			83	542	543
B-0910			80	434	435
B-0911			91	382	383
B-0912			100	396	397
B-0913			94	354	355
B-0914			95	380	381
B-0915			98	494	495

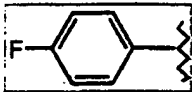
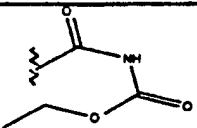
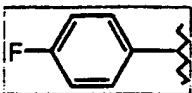
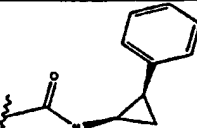
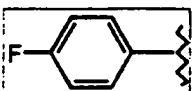
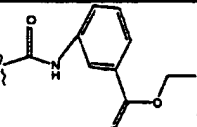
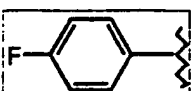
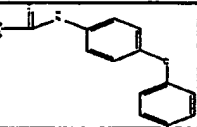
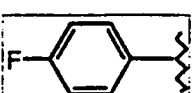
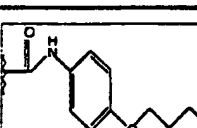
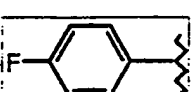
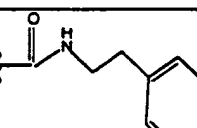
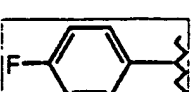
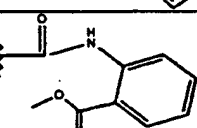
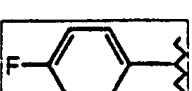
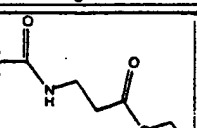
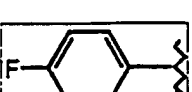
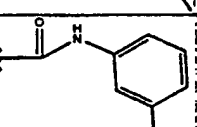
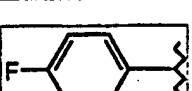
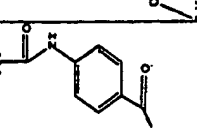
693

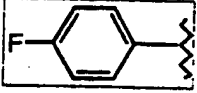
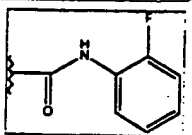
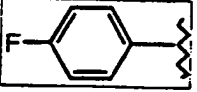
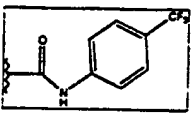
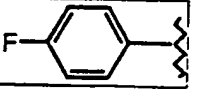
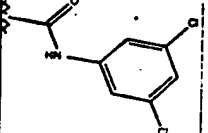
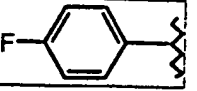
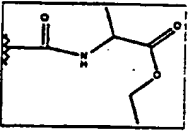
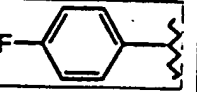
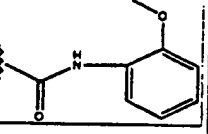
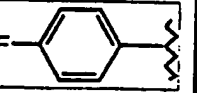
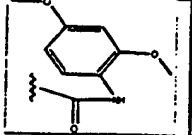
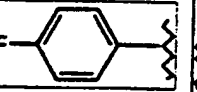
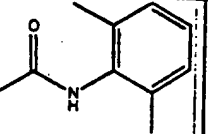
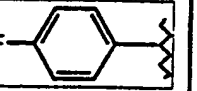
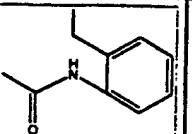
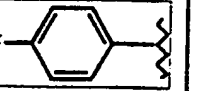
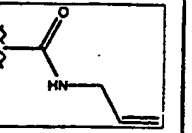
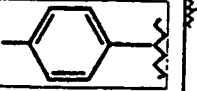
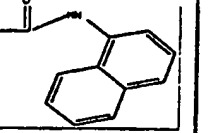
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0916			84	542	543
B-0917			79	407	408
B-0918			89	384	385
B-0919			91	446	447
B-0920			99	460	461
B-0921			84	430	431
B-0922			81	434	435
B-0923			76	417	418
B-0924			70	466	467
B-0925			64	404	405

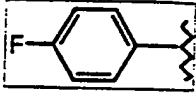
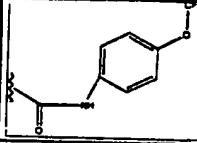
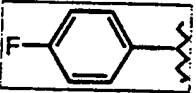
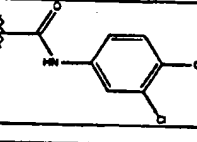
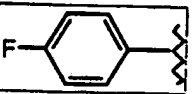
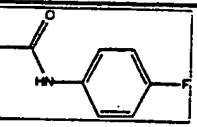
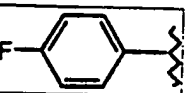
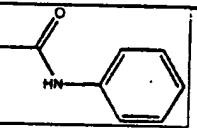
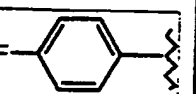
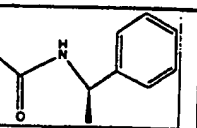
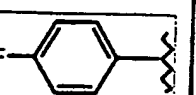
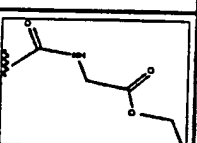
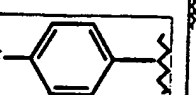
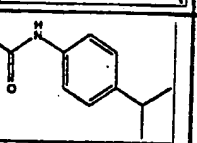
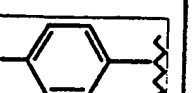
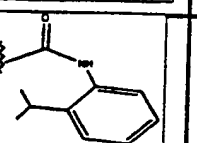
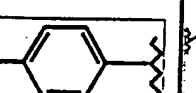
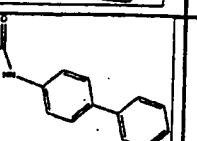
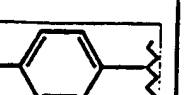
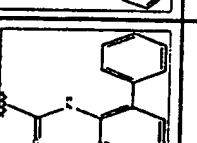
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0926			47	390	391
B-0927			89	470	471
B-0928			53	369	370
B-0929			100	449	450
B-0930			14	459	460
B-0931			41	383	384
B-0932			94	491	492



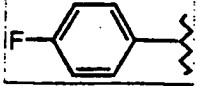
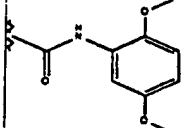
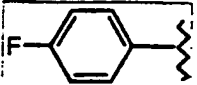
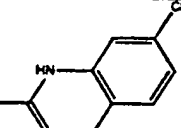
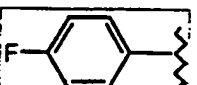
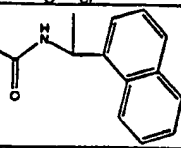
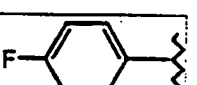
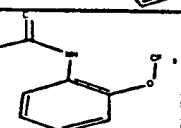
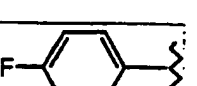
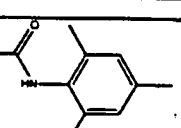
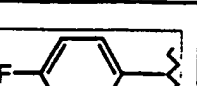
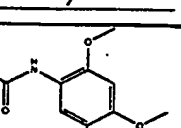
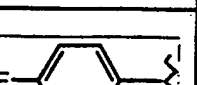
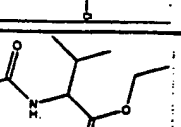

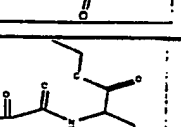



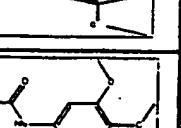
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0933			48	447	448
B-0934			44	429	430
B-0935			33	485	486
B-0936			30	479	-
B-0937			68	367	368
B-0938			72	479	480
B-0939			76	415	416

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0940			36	397	398
B-0941			41	441	442
B-0942			27	473	474
B-0943			55	493	494
B-0944			53	473	474
B-0945			82	429	430
B-0946			100	459	460
B-0947			60	425	426
B-0948			100	431	432
B-0949			98	473	474

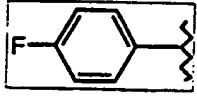
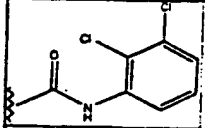
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0950			64	419	420
B-0951			100	469	470
B-0952			61	469	470
B-0953			67	425	426
B-0954			62	431	432
B-0955			39	461	462
B-0956			66	429	430
B-0957			93	429	430
B-0958			86	365	366
B-0959			73	451	452

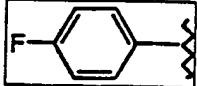
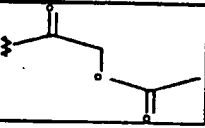
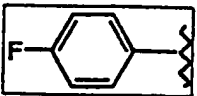
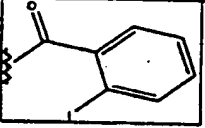
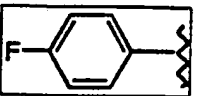
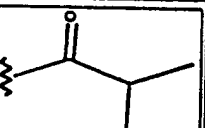
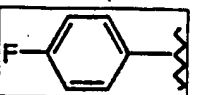
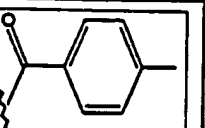
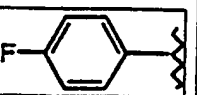
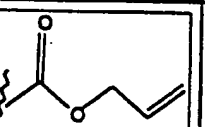
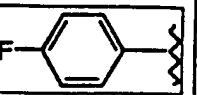
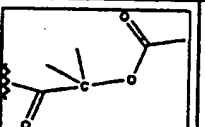
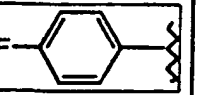
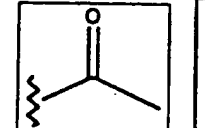
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0960			98	485	486
B-0961			100	469	470
B-0962			100	419	420
B-0963			83	401	402
B-0964			38	429	430
B-0965			90	411	412
B-0966			76	443	444
B-0967			100	443	444
B-0968			100	477	478
B-0969			77	477	478

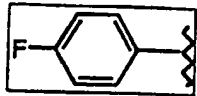
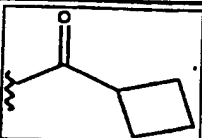
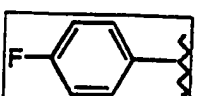
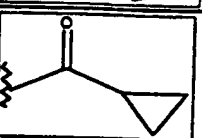
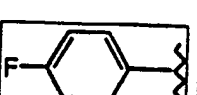
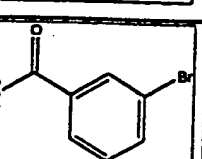
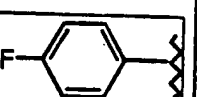
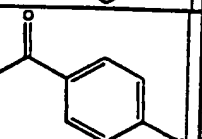
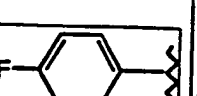
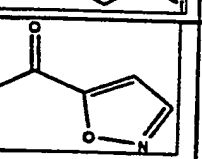
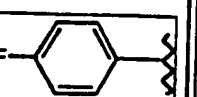
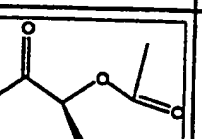
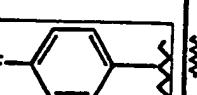
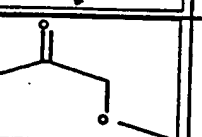
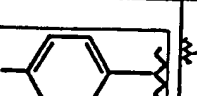
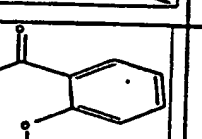
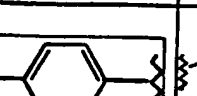
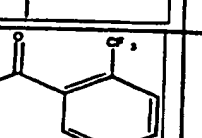


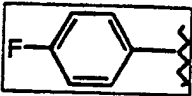
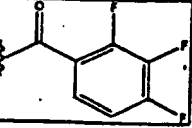
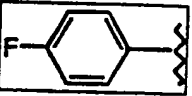
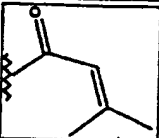
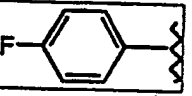
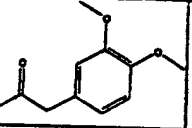
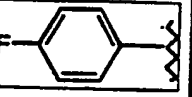
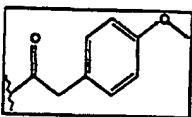
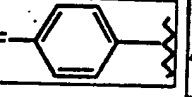
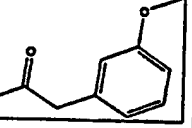
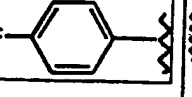
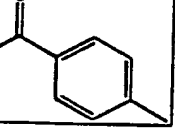
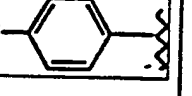
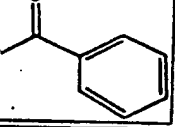
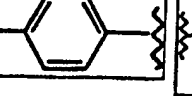
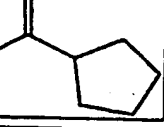
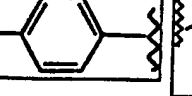
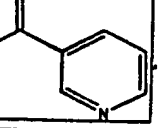
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0970			38	461	462
B-0971			95	469	470
B-0972			98	479	480
B-0973			96	485	486
B-0974			74	443	444
B-0975			100	495	496
B-0976			70	453	454
B-0977			100	467	468
B-0978			91	431	432
B-0979			54	491	492

700

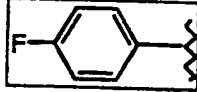
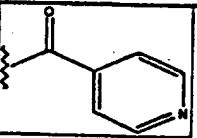
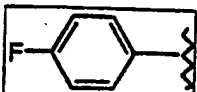
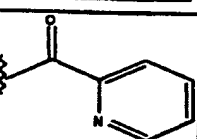
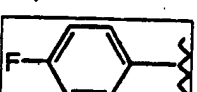
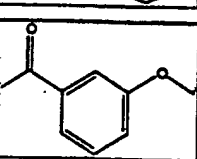
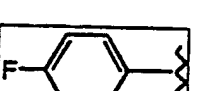
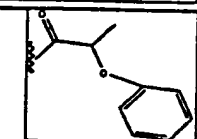
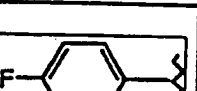
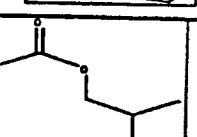

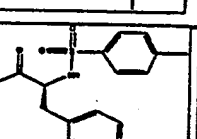

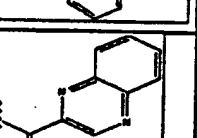
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0980			65	469	470

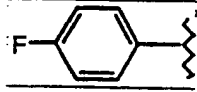
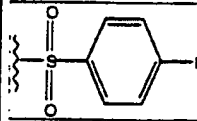
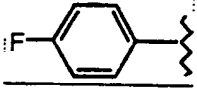
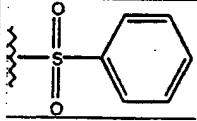
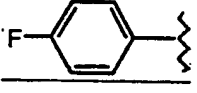
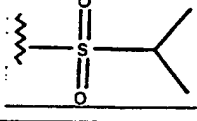
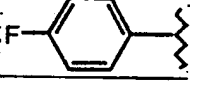
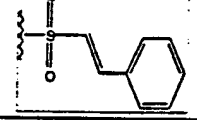
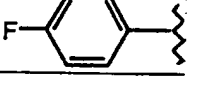
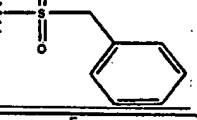
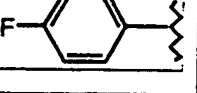
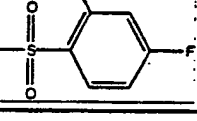
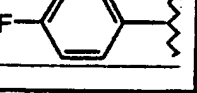
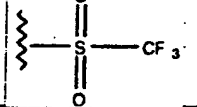
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0981			78	382	383
B-0982			82	512	513
B-0983			94	352	353
B-0984			81	404	405
B-0985			84	366	367
B-0986			80	410	411
B-0987			85	324	325

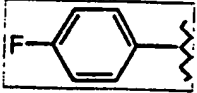
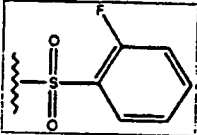
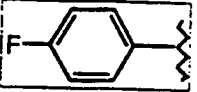
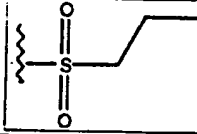
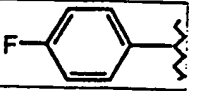
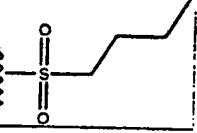
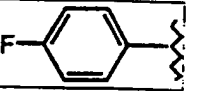
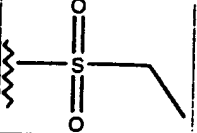
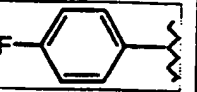
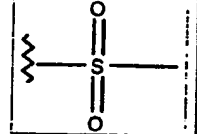
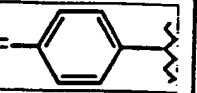
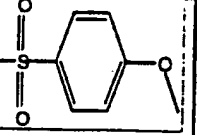
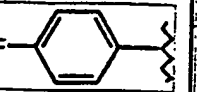
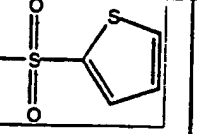
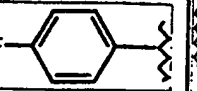
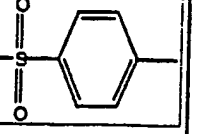
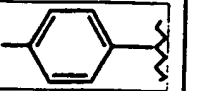
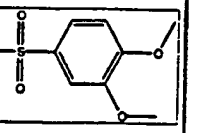
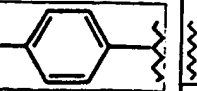
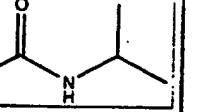
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0988			91	364	365
B-0989			88	350	351
B-0990			68	464	465
B-0991			86	512	513
B-0992			79	377	378
B-0993			81	396	397
B-0994			100	354	355
B-0995			75	416	417
B-0996			65	454	455

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0997			64	440	441
B-0998			81	364	365
B-0999			79	460	461
B-1000			84	430	431
B-1001			78	430	431
B-1002			85	400	401
B-1003			83	386	387
B-1004			87	378	379
B-1005			57	387	388


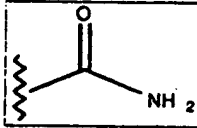
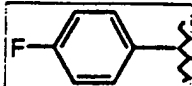
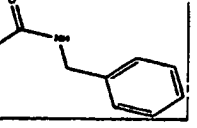
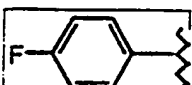
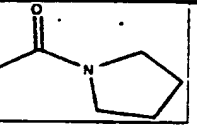
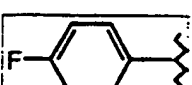
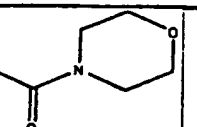
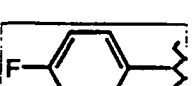
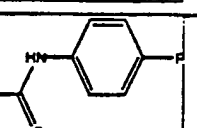
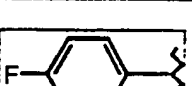
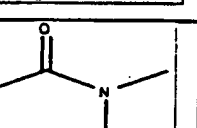

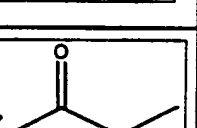

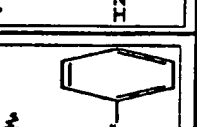

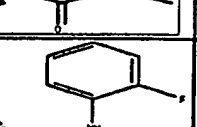

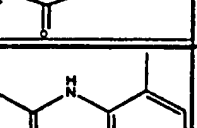
704

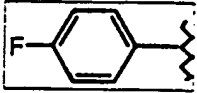
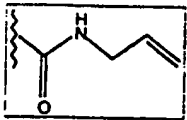
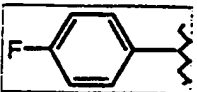
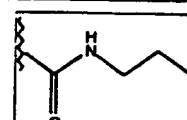
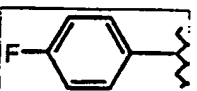
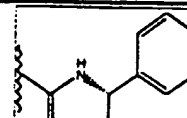
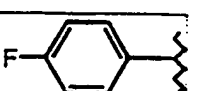
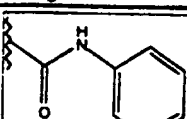
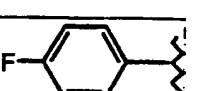

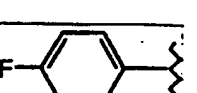
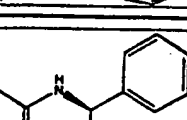
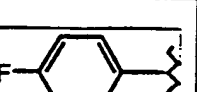
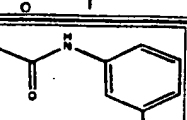
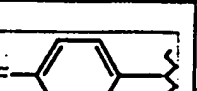
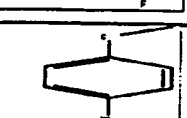
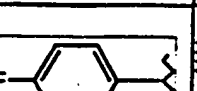

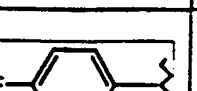

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1006			80	387	388
B-1007			54	387	388
B-1008			64	416	417
B-1009			81	430	431
B-1010			81	382	383
B-1011			66	583	584
B-1012			69	438	439

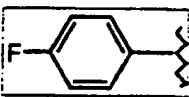
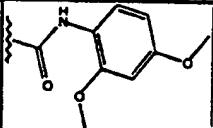
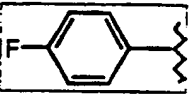
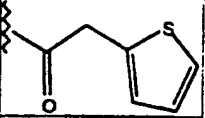
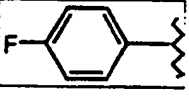
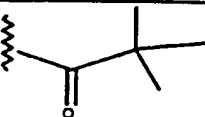
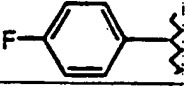
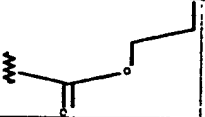
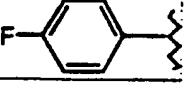
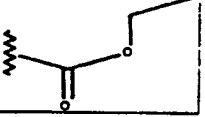
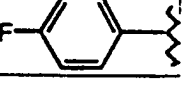
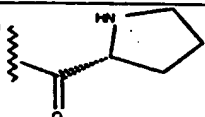
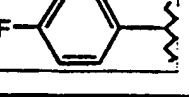
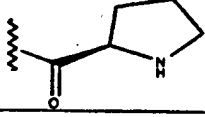
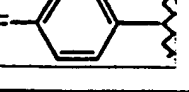
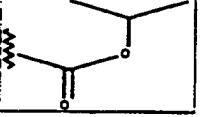
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1013			53	440	441
B-1014			61	422	423
B-1015			47	388	389
B-1016			74	448	449
B-1017			63	436	437
B-1018			82	458	459
B-1019			41	414	415

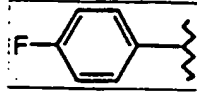
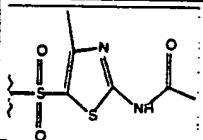
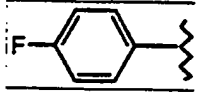
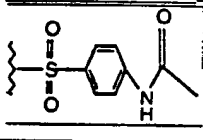
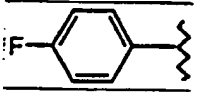
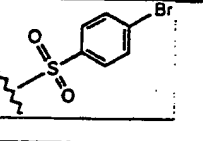
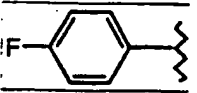
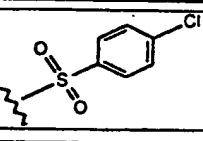
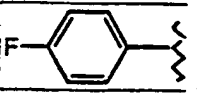
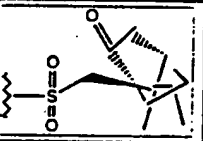
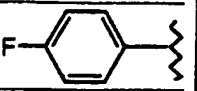
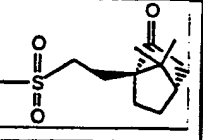
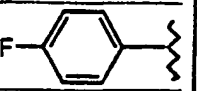
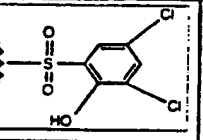
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1020			100	440	441
B-1021			100	388	389
B-1022			74	402	403
B-1023			76	374	375
B-1024			73	360	361
B-1025			100	452	453
B-1026			95	428	429
B-1027			98	436	437
B-1028			100	482	483
B-1029			98	367	368




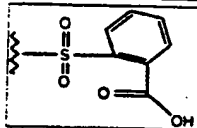
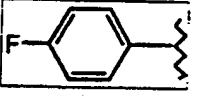
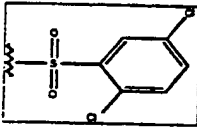
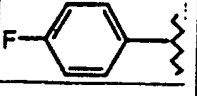
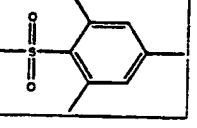
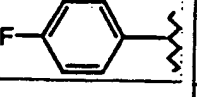
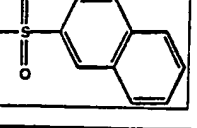
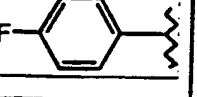
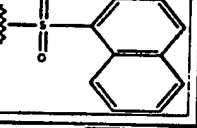
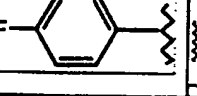
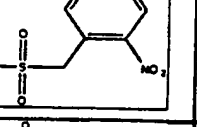
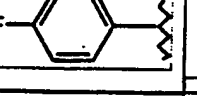
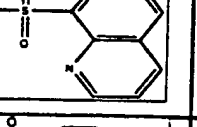
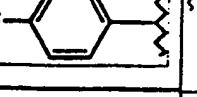
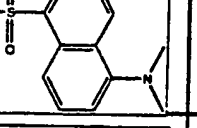
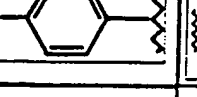
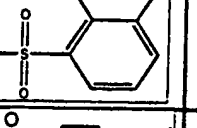
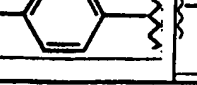
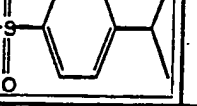
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1030			88	325	326
B-1031			97	415	416
B-1032			64	379	380
B-1033			83	395	396
B-1034			67	419	420
B-1035			73	353	354
B-1036			79	339	340
B-1037			78	415	416
B-1038			100	419	420
B-1039			95	429	430

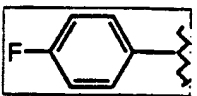
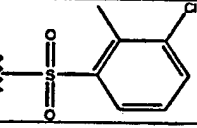
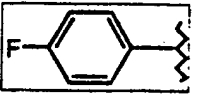
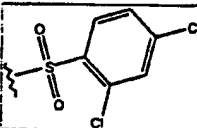
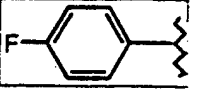
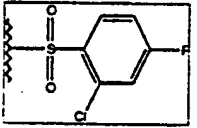
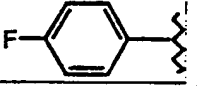
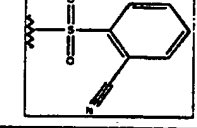
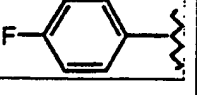
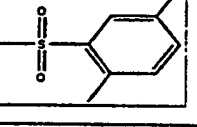
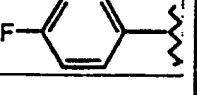
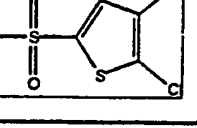
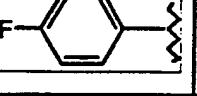
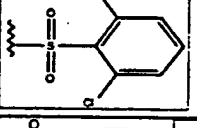
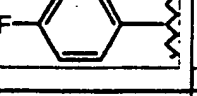
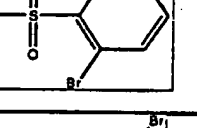
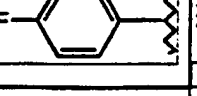
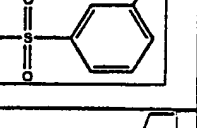
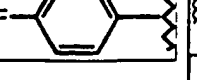
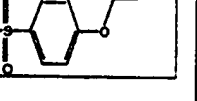
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1040			91	365	366
B-1041			88	367	368
B-1042			78	429	430
B-1043			79	401	402
B-1044			93	429	430
B-1045			100	429	430
B-1046			94	419	420
B-1047			100	431	432
B-1048			58	381	382
B-1049			97	353	354

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1050			100	461	462
B-1051			88	406	407
B-1052			82	366	367
B-1053			21	368	
B-1054			98	354	355
B-1055			100	379	380
B-1056			85	379	380
B-1057			30	368	369

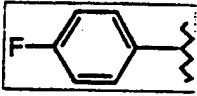
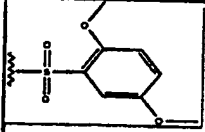
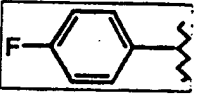
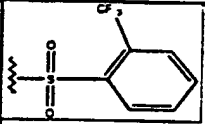
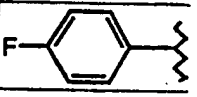
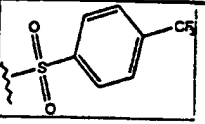
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1058			35	500	501
B-1059			77	479	480
B-1060			37	500	501
B-1061			86	456	457
B-1062			58	496	497
B-1063			59	496	497
B-1064			58	506	-

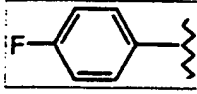
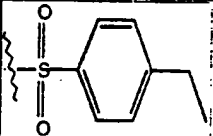
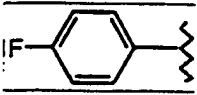
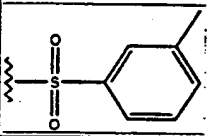
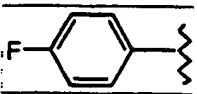
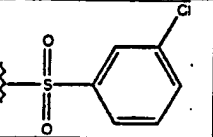
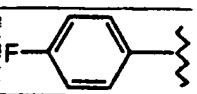
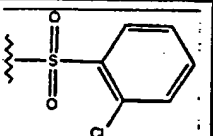
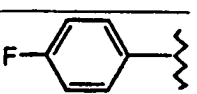
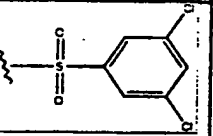
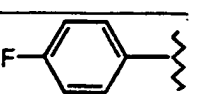
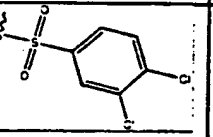
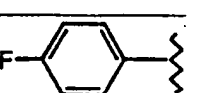
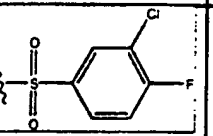
711

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1065			24	466	-
B-1066			100	490	491
B-1067			74	464	465
B-1068			79	472	473
B-1069			97	472	473
B-1070			54	481	482
B-1071			67	473	474
B-1072			35	515	516
B-1073			100	490	491
B-1074			100	464	465

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1075			100	470	471
B-1076			93	490	491
B-1077			100	474	475
B-1078			80	447	448
B-1079			85	454	455
B-1080			100	496	497
B-1081			100	490	491
B-1082			100	500	501
B-1083			93	500	501
B-1084			81	494	495


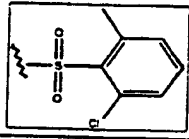
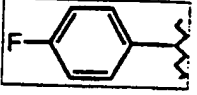
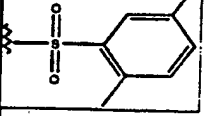
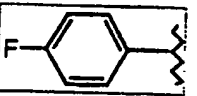
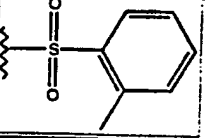
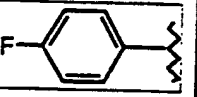
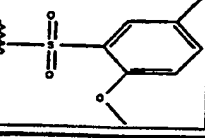
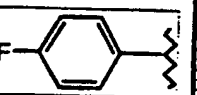
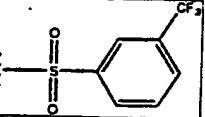
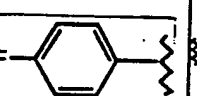
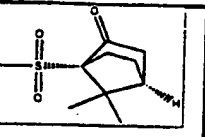
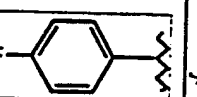
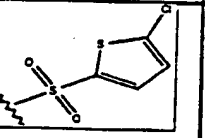
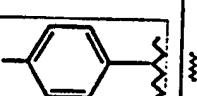
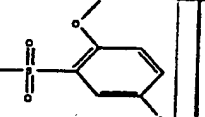
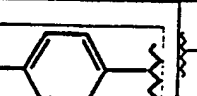
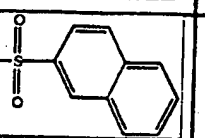
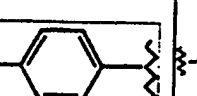
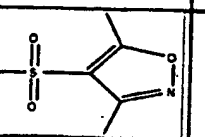
713

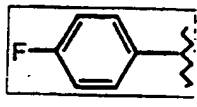
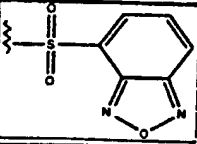
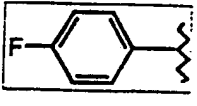
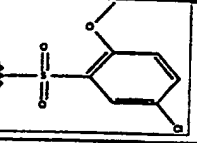
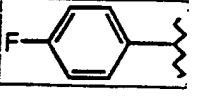
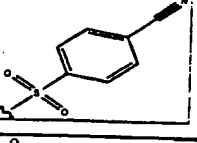
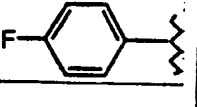
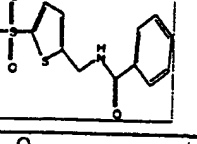
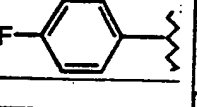

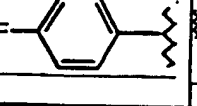
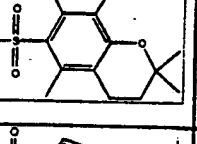
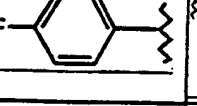
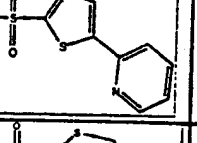
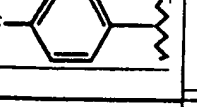
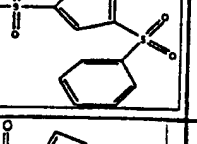
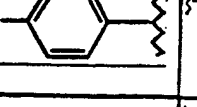
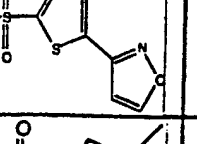
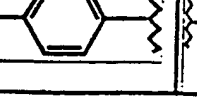
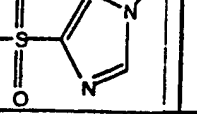
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1085			93	482	483
B-1086			92	490	491
B-1087			100	490	491

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1088			97	450	451
B-1089			100	436	437
B-1090			100	456	457
B-1091			100	456	457
B-1092			96	490	491
B-1093			100	490	491
B-1094			100	474	475

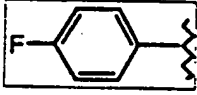
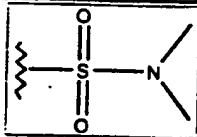
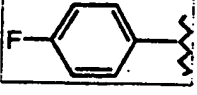
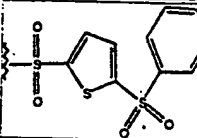
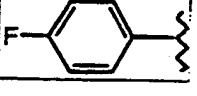
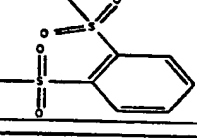
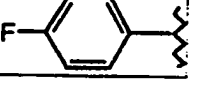
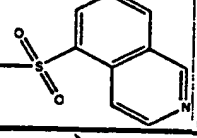
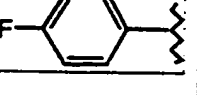
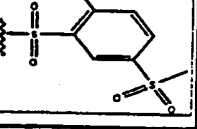


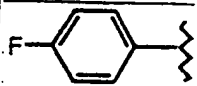
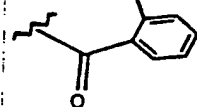
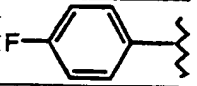
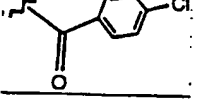
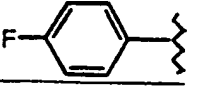
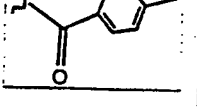
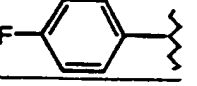
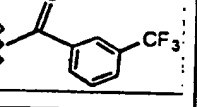
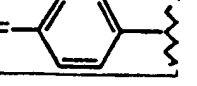
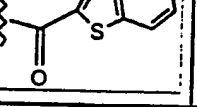
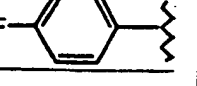
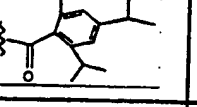
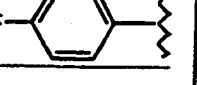
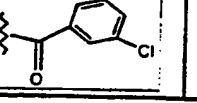
715

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1095			81	470	471
B-1096			77	450	451
B-1097			100	436	437
B-1098			93	466	467
B-1099			100	490	491
B-1100			47	482	-
B-1101			64	462	463
B-1102			98	530	531
B-1103			65	472	-
B-1104			88	441	442

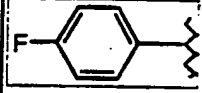
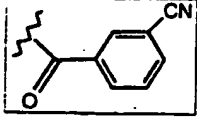
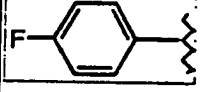
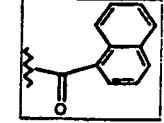
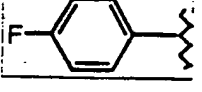
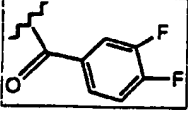
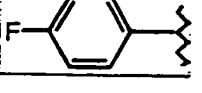
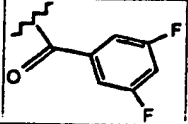
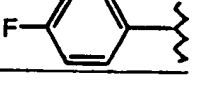
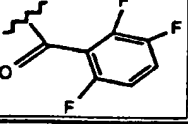
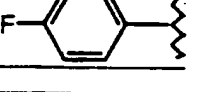
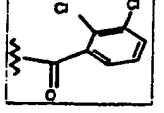
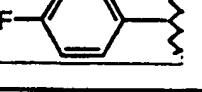
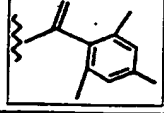
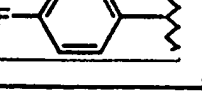
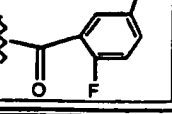
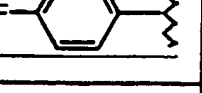
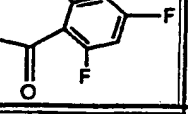
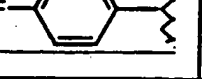
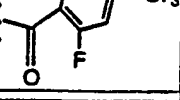
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1105			100	464	465
B-1106			91	486	487
B-1107			96	447	448
B-1108			55	561	562
B-1109			100	498	499
B-1110			73	548	549
B-1111			94	505	506
B-1112			100	568	569
B-1113			100	495	496
B-1114			73	426	427

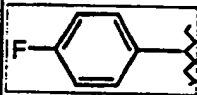
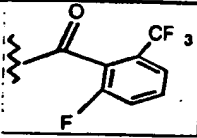
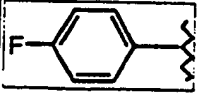
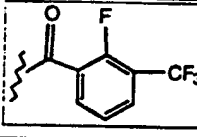
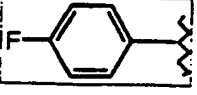
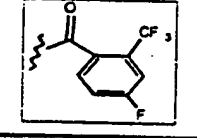
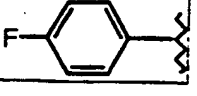
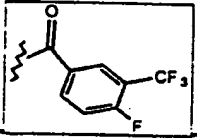
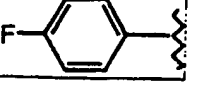
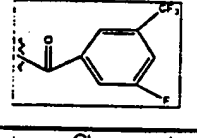
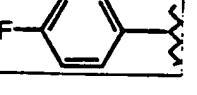
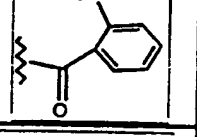
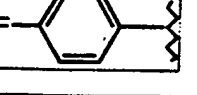
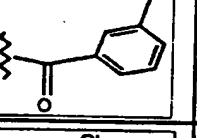
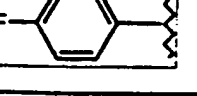
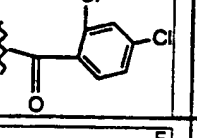
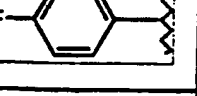
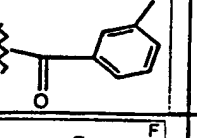
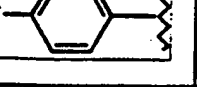
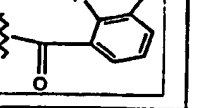
717

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1115			30	389	390
B-1116			100	568	569
B-1117			83	500	501
B-1118			55	473	-
B-1119			70	514	515

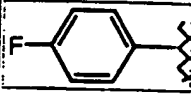
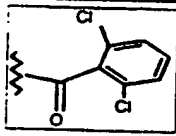
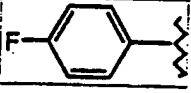
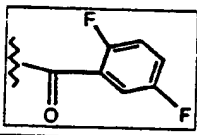
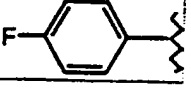
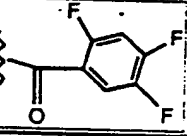
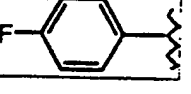
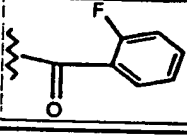
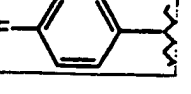
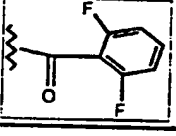
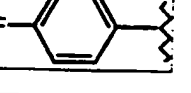
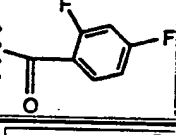
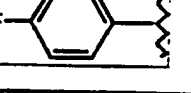
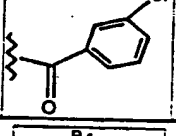
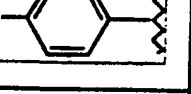
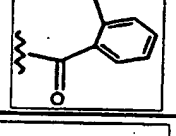
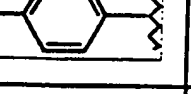
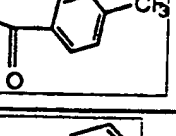
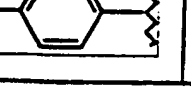
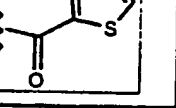
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1120			84	400	401
B-1121			86	420	421
B-1122			90	400	401
B-1123			100	454	455
B-1124			91	442	443
B-1125			50	512	513
B-1126			85	454	455

719

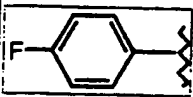
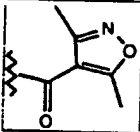
Example#	R <sup>2</sup>	R <sup>4</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1127			93	411	412
B-1128			87	436	437
B-1129			78	422	423
B-1130			96	422	423
B-1131			84	440	441
B-1132			77	454	455
B-1133			62	428	429
B-1134			91	472	473
B-1135			85	440	441
B-1136			82	472	473

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1137			95	472	473
B-1138			100	472	473
B-1139			100	472	473
B-1140			92	472	473
B-1141			100	472	473
B-1142			88	420	421
B-1143			90	400	401
B-1144			87	454	455
B-1145			93	404	405
B-1146			90	422	423

721

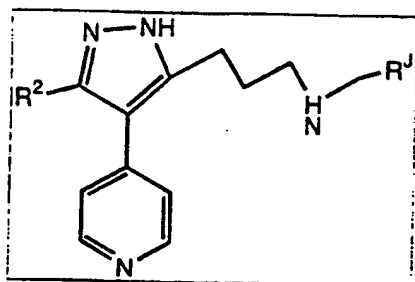
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1147			100	454	455
B-1148			87	422	423
B-1149			87	440	441
B-1150			90	404	405
B-1151			82	422	423
B-1152			85	422	423
B-1153			90	420	421
B-1154			78	464	465
B-1155			79	454	455
B-1156			95	392	393

722

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1157			81	405	406

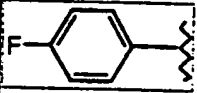
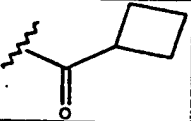
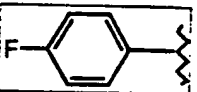
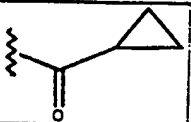
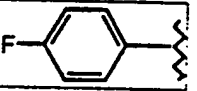
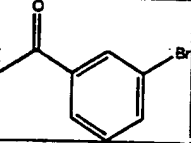
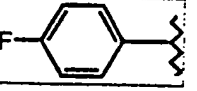
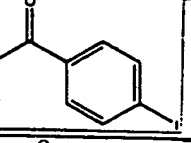
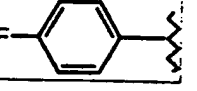
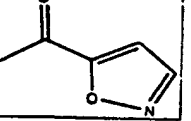
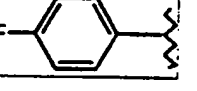
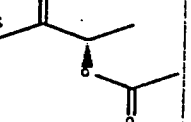
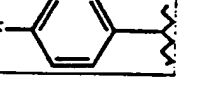
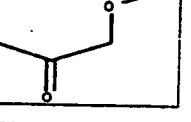
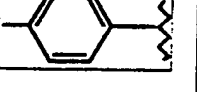
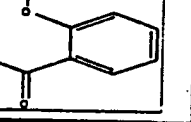
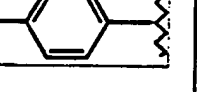
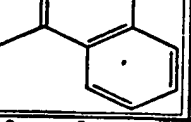
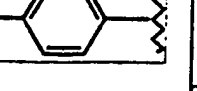
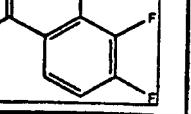


723


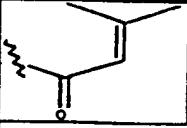
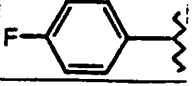
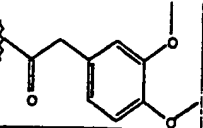
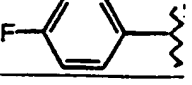
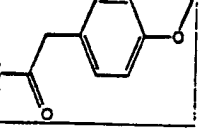
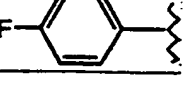
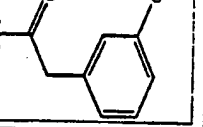
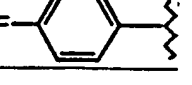
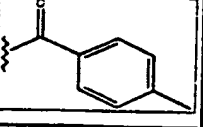
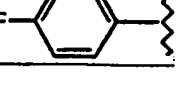
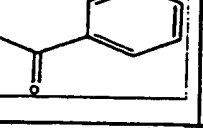
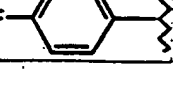
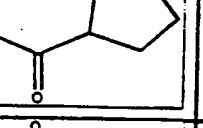
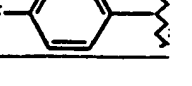
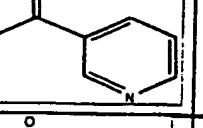
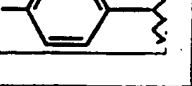
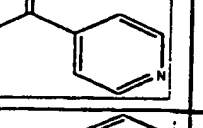
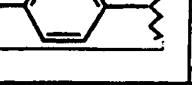
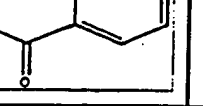


Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1158			54	396	397
B-1159			42	526	527
B-1160			27	366	367
B-1161			58	418	419
B-1162			62	380	381
B-1163			58	424	425
B-1164			67	338	339

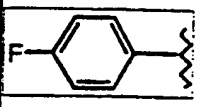
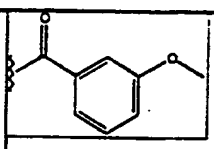
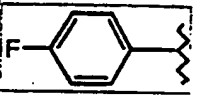
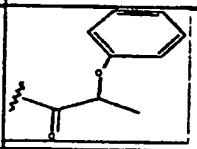
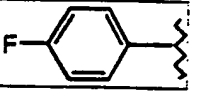
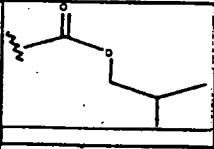
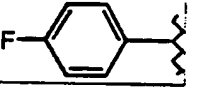
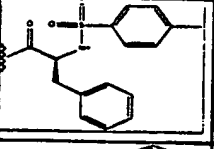
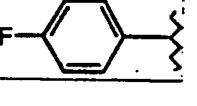
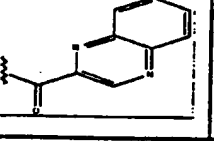
724

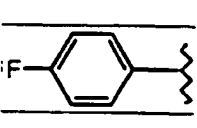
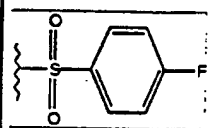
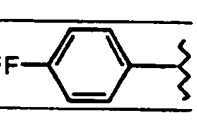
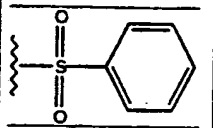
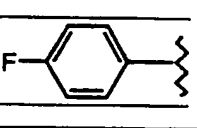
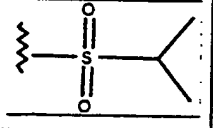
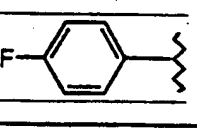
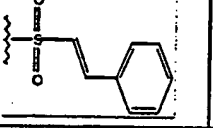
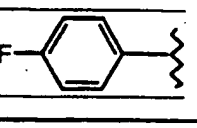
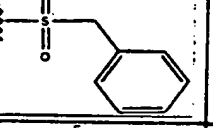
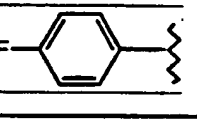
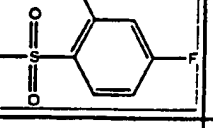
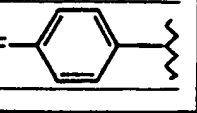
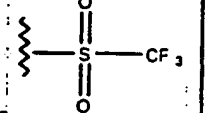
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1165			66	378	379
B-1166			65	364	365
B-1167			64	478	479
B-1168			76	526	527
B-1169			70	391	392
B-1170			76	410	411
B-1171			82	368	369
B-1172			73	430	431
B-1173			74	468	469
B-1174			83	454	455

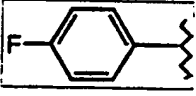
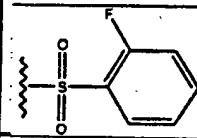
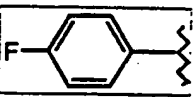
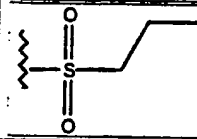
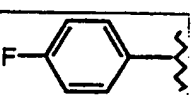
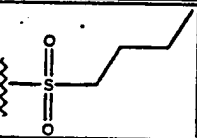
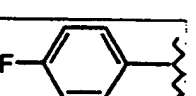
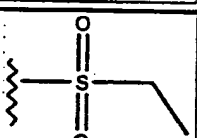
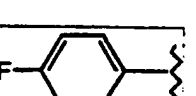
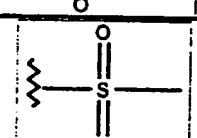
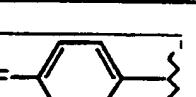
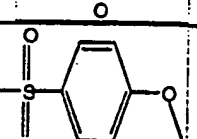

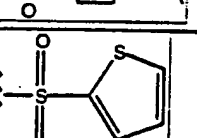
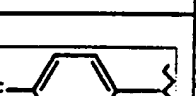
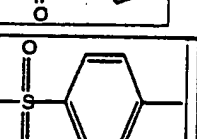

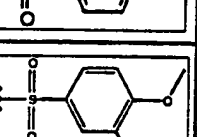

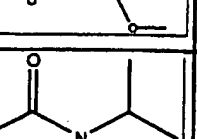
725

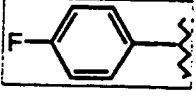
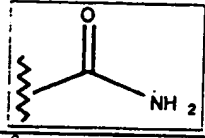
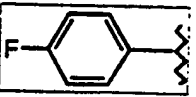

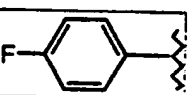
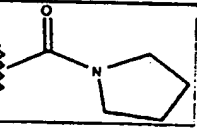
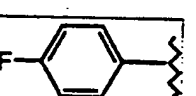
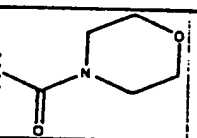
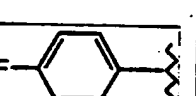
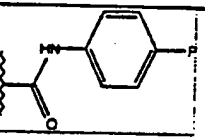
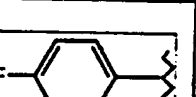
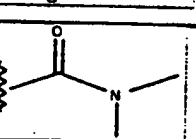
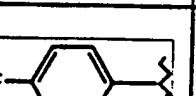
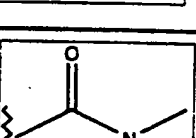
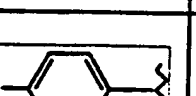
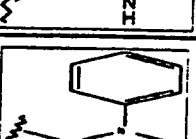

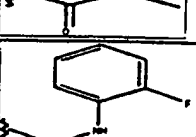

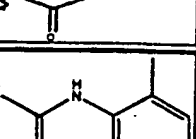
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1175			76	378	379
B-1176			96	474	475
B-1177			94	444	445
B-1178			90	444	445
B-1179			57	414	415
B-1180			75	400	401
B-1181			66	392	393
B-1182			74	401	402
B-1183			62	401	402
B-1184			51	401	402

726

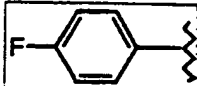
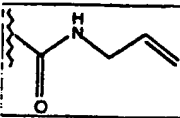
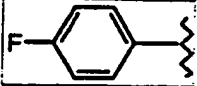
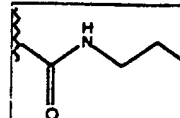
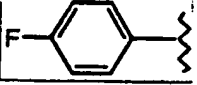
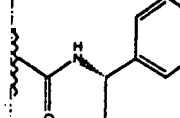
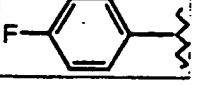
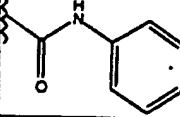
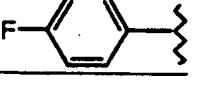
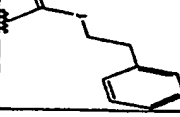
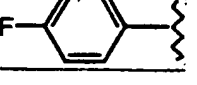
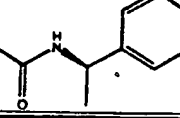
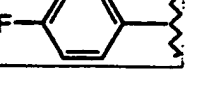
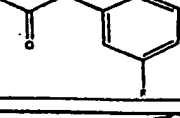
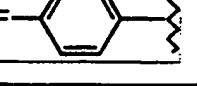

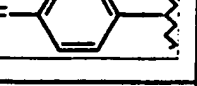
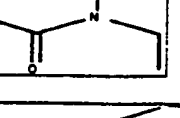
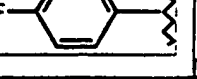
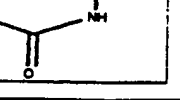
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1185			90	430	431
B-1186			86	444	445
B-1187			74	396	397
B-1188			76	597	598
B-1189			60	452	453

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1190			44	454	455
B-1191			47	436	437
B-1192			50	402	403
B-1193			62	462	463
B-1194			49	450	451
B-1195			61	472	473
B-1196			52	428	429

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1197			54	454	455
B-1198			44	402	403
B-1199			67	416	417
B-1200			45	388	389
B-1201			52	374	375
B-1202			100	466	467
B-1203			91	442	443
B-1204			100	450	451
B-1205			83	496	497
B-1206			97	381	382

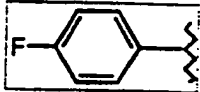
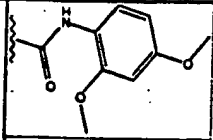
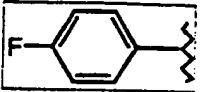
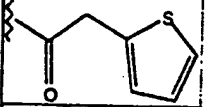
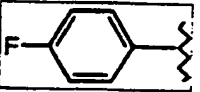
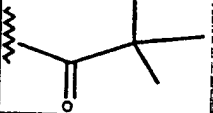
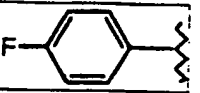
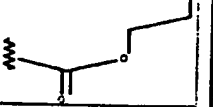
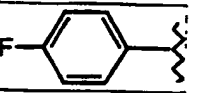
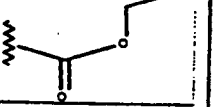
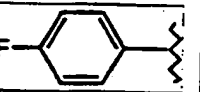
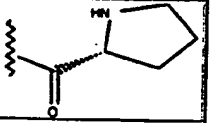
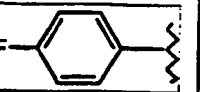
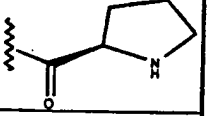
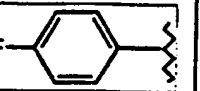
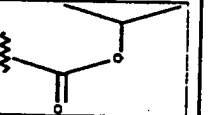
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1207			100	339	340
B-1208			90	429	430
B-1209			69	393	394
B-1210			35	409	410
B-1211			100	433	434
B-1212			83	367	368
B-1213			78	353	354
B-1214			68	429	430
B-1215			65	433	434
B-1216			91	443	444

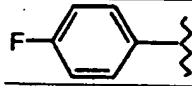
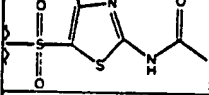
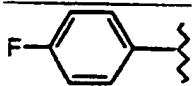
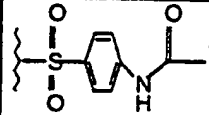
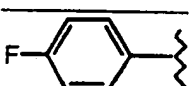
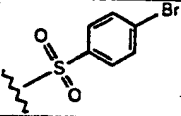
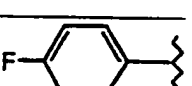
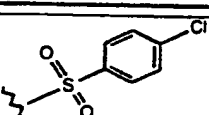
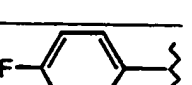
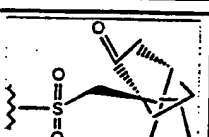
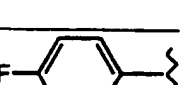
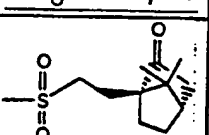

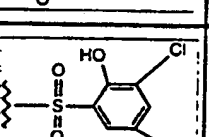
730

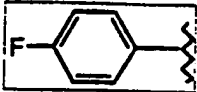
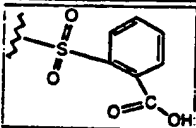
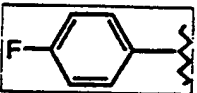
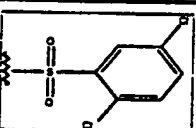
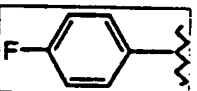
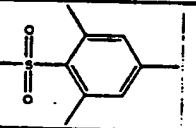
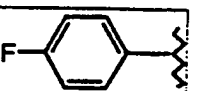
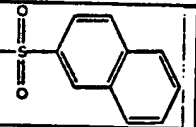
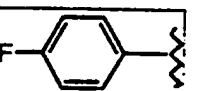
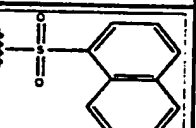
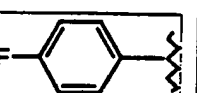
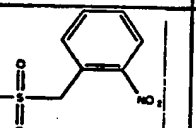
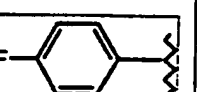
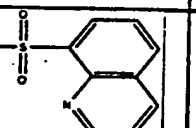
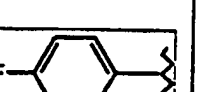
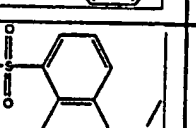
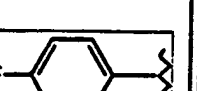
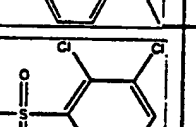
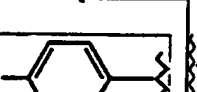
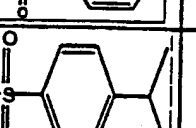
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1217			99	379	380
B-1218			92	381	382
B-1219			74	443	444
B-1220			67	415	416
B-1221			14	443	444
B-1222			19	443	444
B-1223			71	433	434
B-1224			100	445	446
B-1225			75	395	396
B-1226			58	367	368

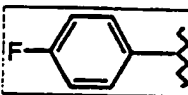
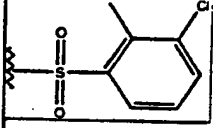
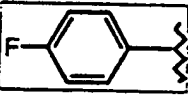
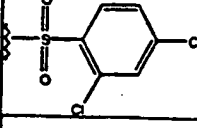
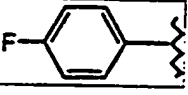
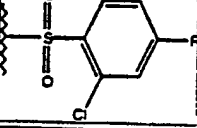
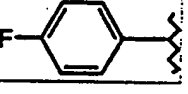
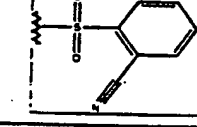
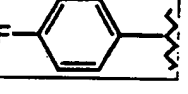
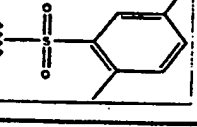
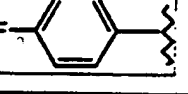
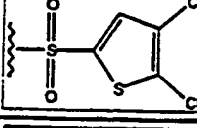

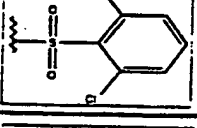
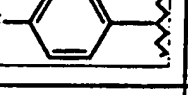
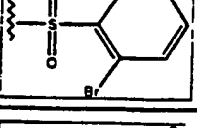
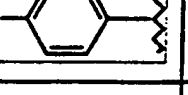
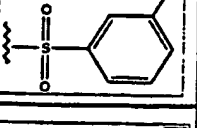
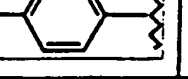
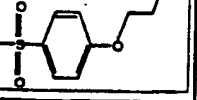


731

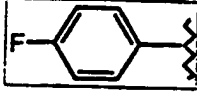
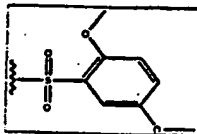
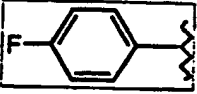
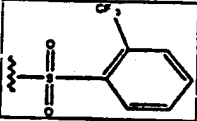
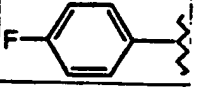
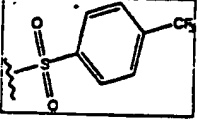
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1227			98	475	476
B-1228			71	420	421
B-1229			85	380	381
B-1230			10	382	-
B-1231			66	368	369
B-1232			100	393	394
B-1233			96	393	394
B-1234			66	382	383

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1235			50	514	515
B-1236			100	493	494
B-1237			91	514	515
B-1238			100	470	471
B-1239			71	510	511
B-1240			27	510	511
B-1241			73	520	

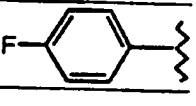
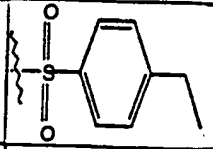
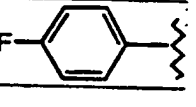
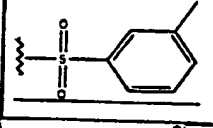
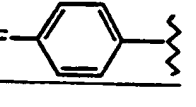
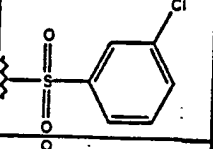
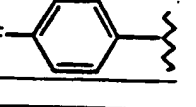
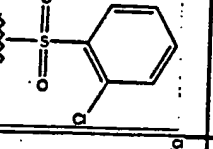
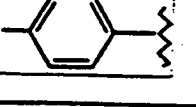
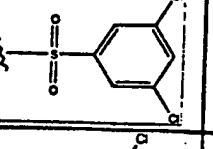
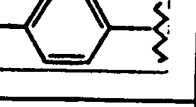
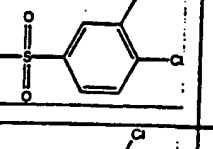
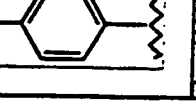
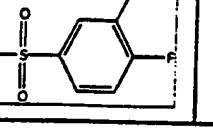
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1242			26	480	481
B-1243			100	504	
B-1244			52	478	479
B-1245			100	486	487
B-1246			56	486	487
B-1247			43	495	496
B-1248			61	487	488
B-1249			32	529	530
B-1250			56	504	505
B-1251			58	478	479

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1252			98	484	485
B-1253			59	504	505
B-1254			100	488	489
B-1255			96	461	
B-1256			79	468	469
B-1257			63	510	511
B-1258			100	504	505
B-1259			95	514	515
B-1260			92	514	515
B-1261			98	508	509

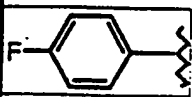
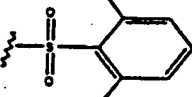
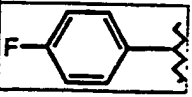
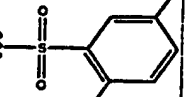
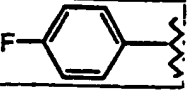
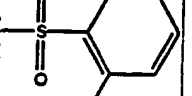
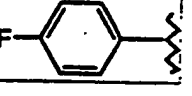
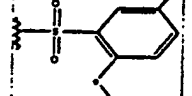
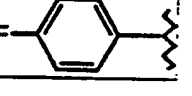
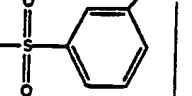
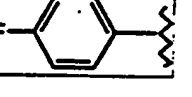
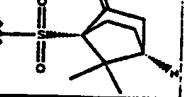
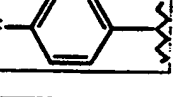
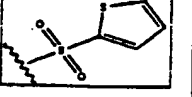

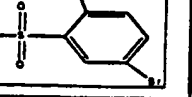
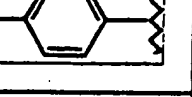
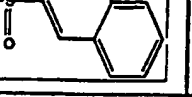
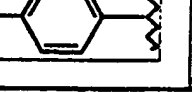
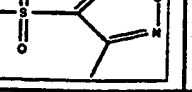
735

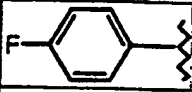
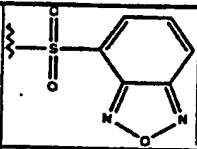
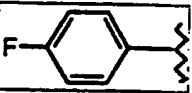
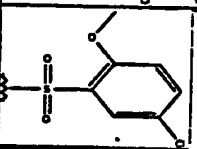
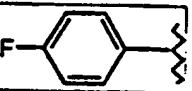
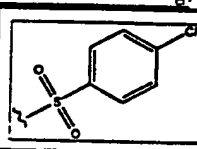
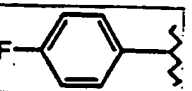
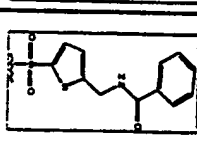
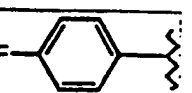
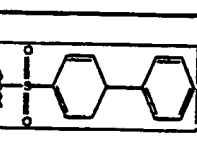
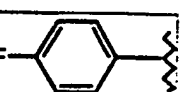
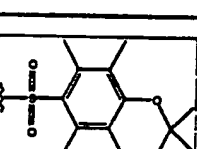
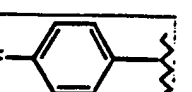
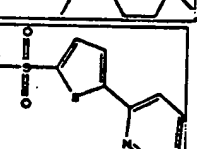
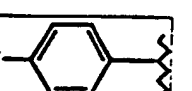
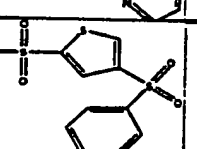
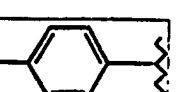
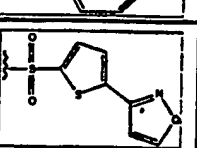
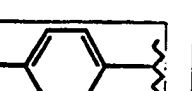
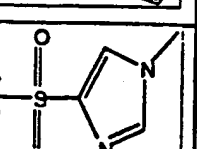
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1262			97	496	497
B-1263			100	504	505
B-1264			100	504	505

736

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1265			100	464	465
B-1266			79	466	451
B-1267			100	470	471
B-1268			87	470	471
B-1269			100	504	505
B-1270			100	504	505
B-1271			56	488	489

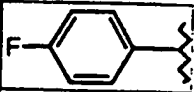
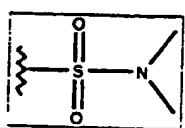
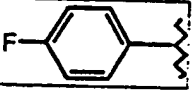
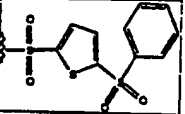
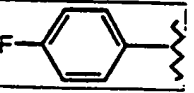
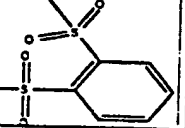
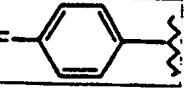
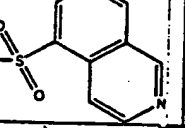
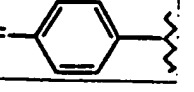
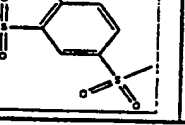
737

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1272			98	484	485
B-1273			90	464	465
B-1274			87	450	451
B-1275			94	480	481
B-1276			100	504	505
B-1277			60	496	511
B-1278			68	476	477
B-1279			100	544	545
B-1280			68	486	-
B-1281			98	455	456

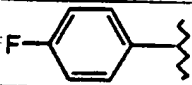
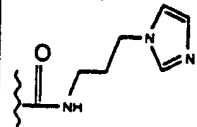
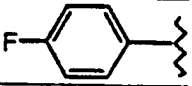
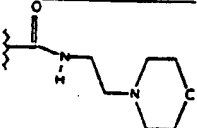
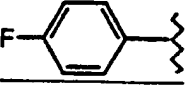
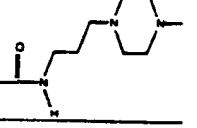
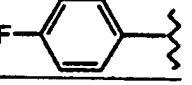
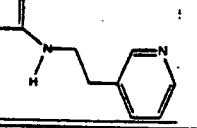
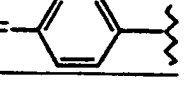
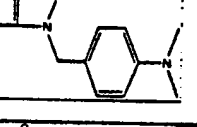
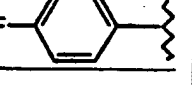
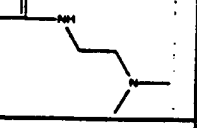
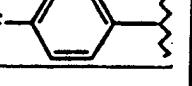
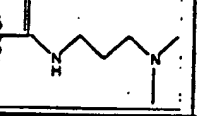
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1282			100	478	479
B-1283			58	500	501
B-1284			58	461	462
B-1285			65	575	576
B-1286			87	512	513
B-1287			79	562	563
B-1288			100	519	520
B-1289			77	582	583
B-1290			100	509	510
B-1291			91	440	441



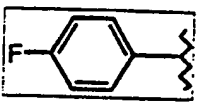
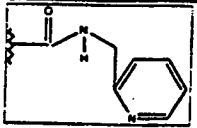
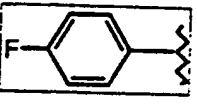
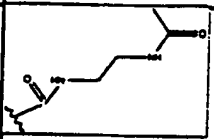
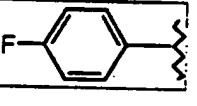
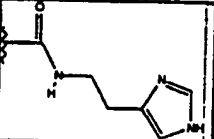
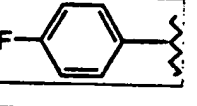
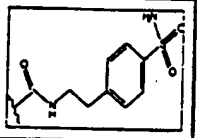
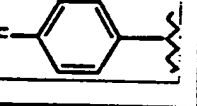
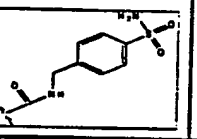
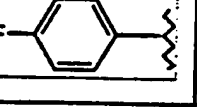
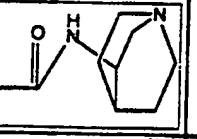
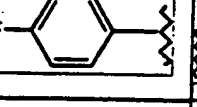
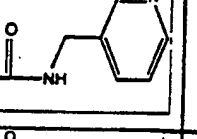
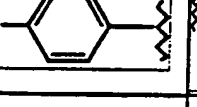
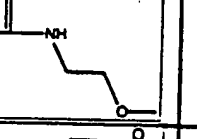

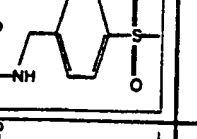
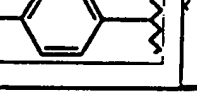
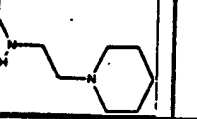
739

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1292			35	403	404
B-1293			73	582	583
B-1294			49	514	515
B-1295			48	487	-
B-1296			76	528	529

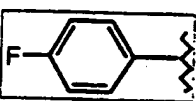
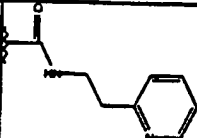
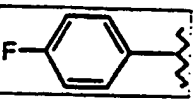
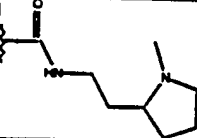
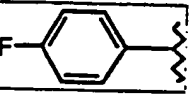
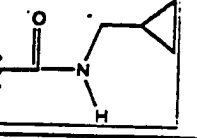
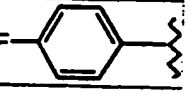
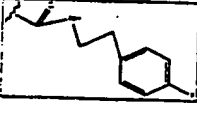
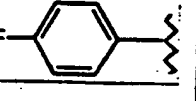
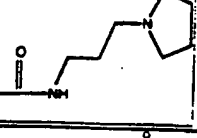
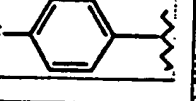
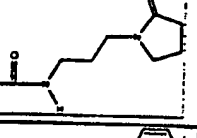
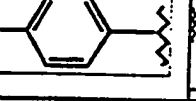
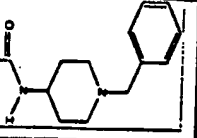
740

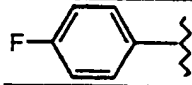
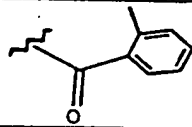
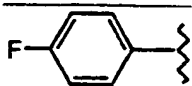
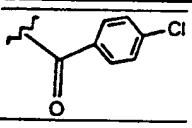
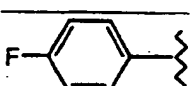
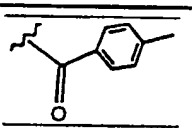
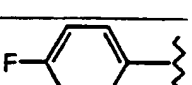
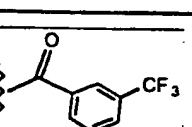
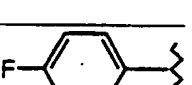
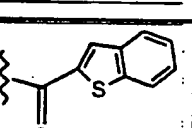
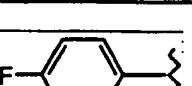
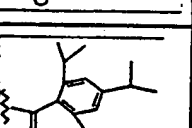

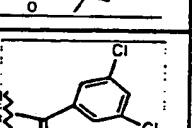
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1297			62	447	448
B-1298			66	452	453
B-1299			65	479	431
B-1300			71	444	445
B-1301			100	472	473
B-1302			75	410	411
B-1303			74	424	425

741

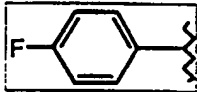
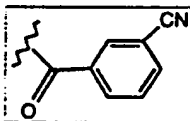
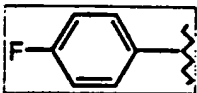
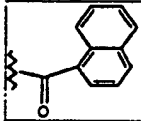
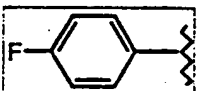
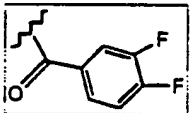
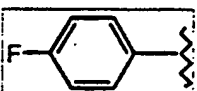
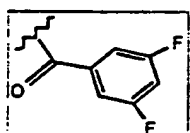
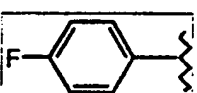
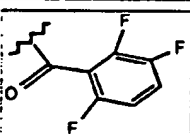
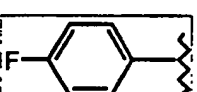
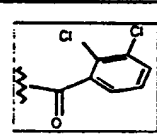
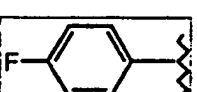
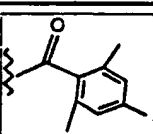
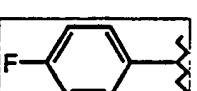
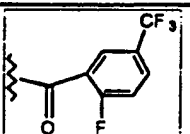
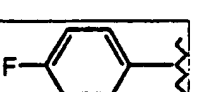
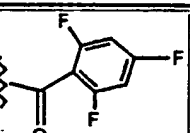
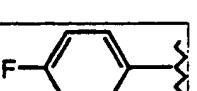
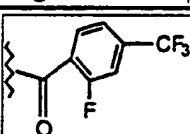
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1304			11	430	431
B-1305			2	424	-
B-1306			30	433	434
B-1307			100	522	523
B-1308			100	508	509
B-1309			100	448	449
B-1310			26	430	431
B-1311			45	397	398
B-1312			14	507	508
B-1313			67	450	451

742

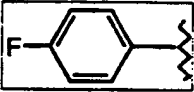
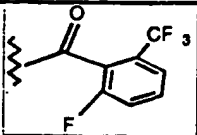
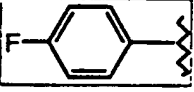
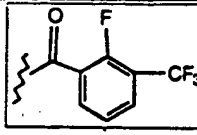
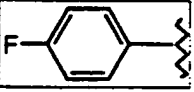
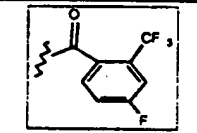
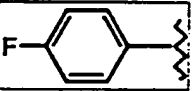
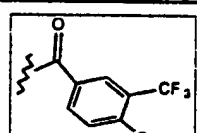
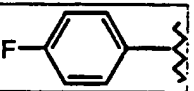
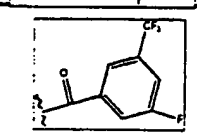
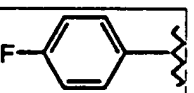
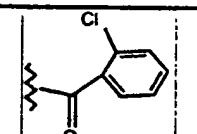
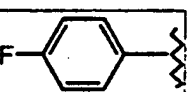
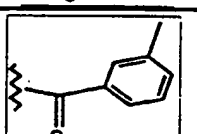
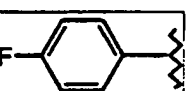
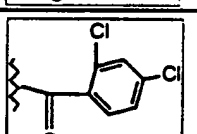
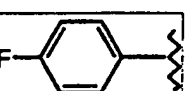
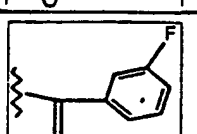
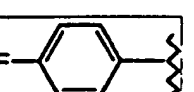
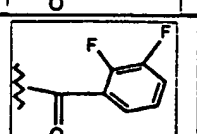
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1314			69	444	445
B-1315			57	450	451
B-1316			75	393	394
B-1317			100	461	462
B-1318			31	450	451
B-1319			23	464	465
B-1320			59	512	513

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1321			63	414	415
B-1322			45	434	435
B-1323			53	414	415
B-1324			32	468	469
B-1325			45	456	457
B-1326			50	526	527
B-1327			55	468	469

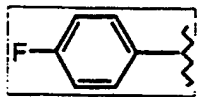
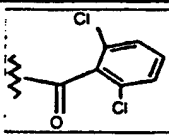
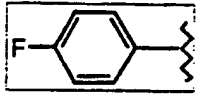
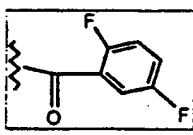
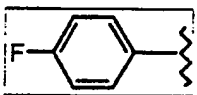
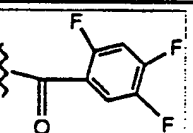
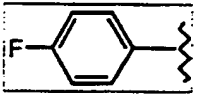
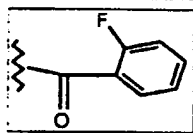
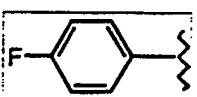
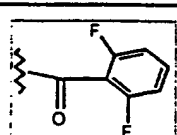
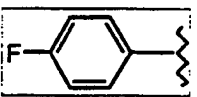
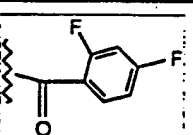
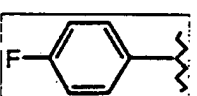
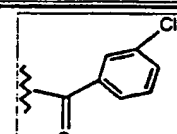
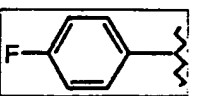
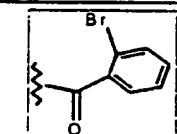
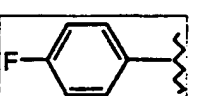
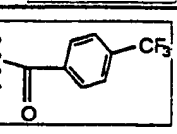
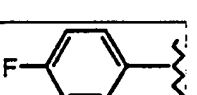
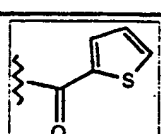
744

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1328			29	425	426
B-1329			67	450	451
B-1330			59	436	437
B-1331			45	436	437
B-1332			81	454	455
B-1333			23	468	469
B-1334			53	442	443
B-1335			81	486	487
B-1336			69	454	455
B-1337			67	486	487

745

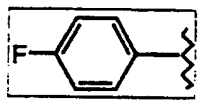
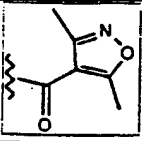
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1338			39	486	487
B-1339			61	486	487
B-1340			49	486	487
B-1341			55	486	487
B-1342			51	486	487
B-1343			72	434	435
B-1344			52	414	415
B-1345			43	468	469
B-1346			40	418	419
B-1347			67	436	437

746

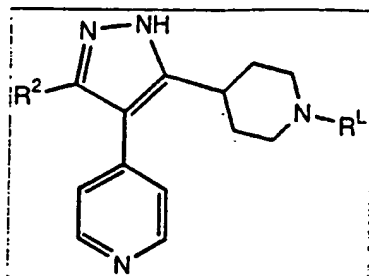
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1348			39	468	469
B-1349			68	436	437
B-1350			73	454	455
B-1351			54	418	419
B-1352			77	436	437
B-1353			66	436	437
B-1354			58	434	435
B-1355			77	478	479
B-1356			50	468	469
B-1357			36	406	407



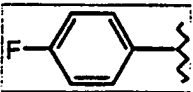
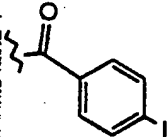
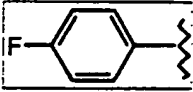
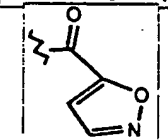
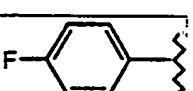
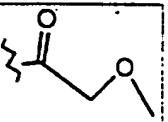
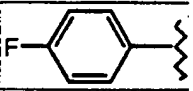
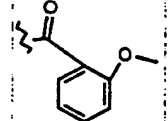
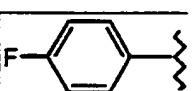
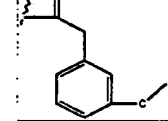
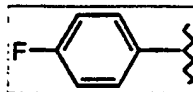
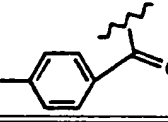
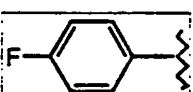
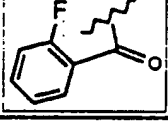
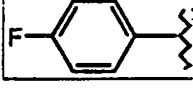
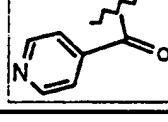
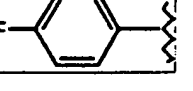
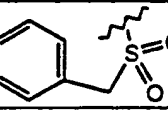
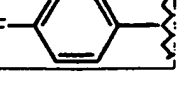
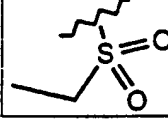
747

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1358			39	419	420

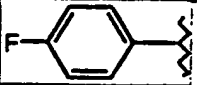
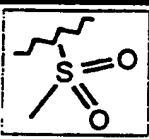
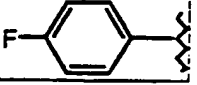
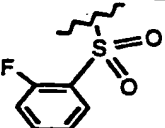
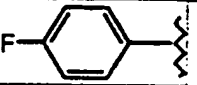
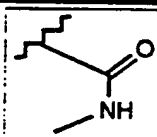
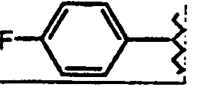
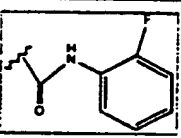
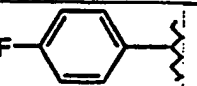
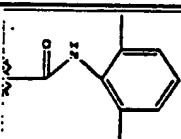
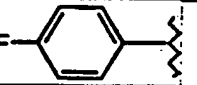
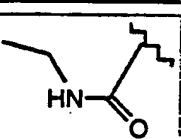
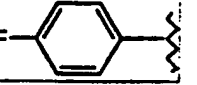
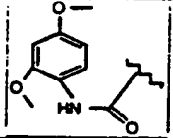
748



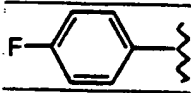
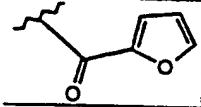
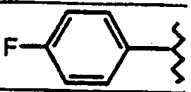
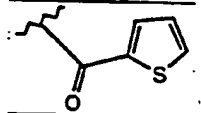
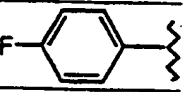
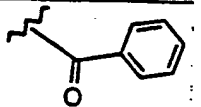
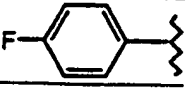
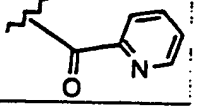
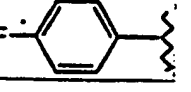
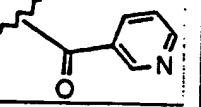
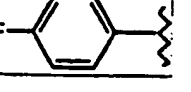
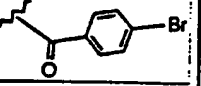
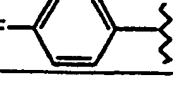
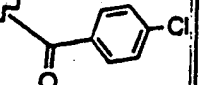
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1359			95	552	553
B-1360			77	444	445
B-1361			100	392	393
B-1362			85	406	407
B-1363			100	364	365
B-1364			99	390	391
B-1365			92	504	505

Example#	R <sup>2</sup>	R <sup>4</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1366			100	552	553
B-1367			100	417	418
B-1368			86	394	395
B-1369			100	456	457
B-1370			100	470	471
B-1371			77	440	441
B-1372			100	444	445
B-1373			42	427	428
B-1374			60	476	477
B-1375			94	414	415

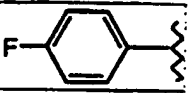
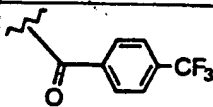
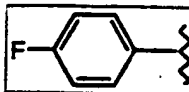
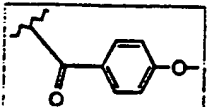
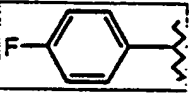
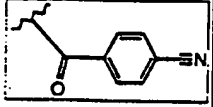
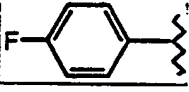
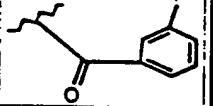
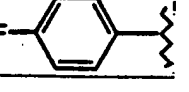
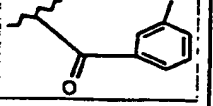
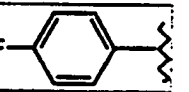
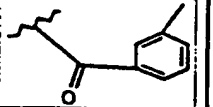
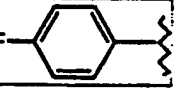
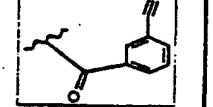
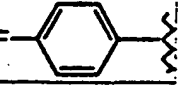
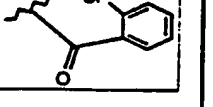
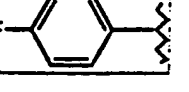
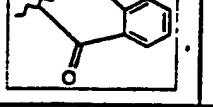
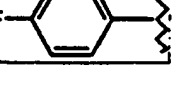
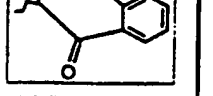
750

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1376			87	400	401
B-1377			100	480	481
B-1378			95	379	380
B-1379			93	459	460
B-1380			89	469	470
B-1381			84	393	394
B-1382			85	501	502


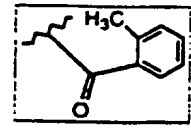
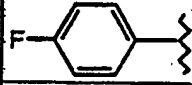
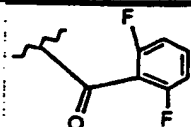
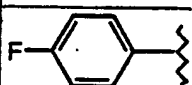
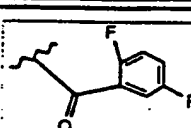
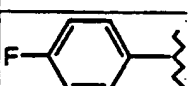
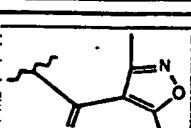
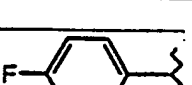
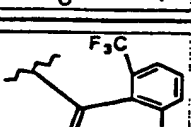

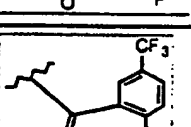

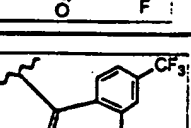

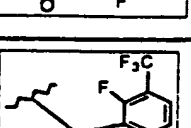

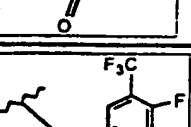

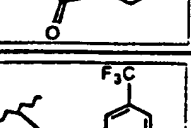
751

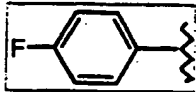
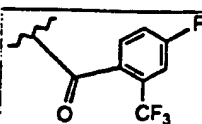
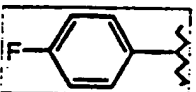
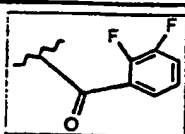
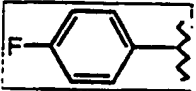
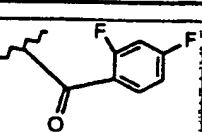
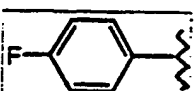
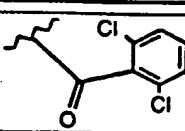
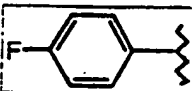
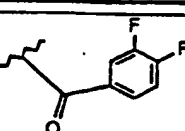
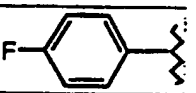
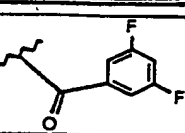
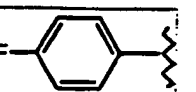
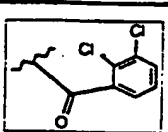
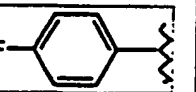
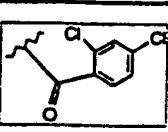
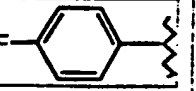
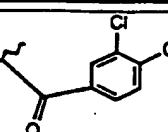
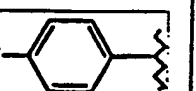
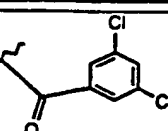
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1383			46	416	417
B-1384			56	432	433
B-1385			59	426	427
B-1386			50	427	428
B-1387			12	427	428
B-1388			66	504	505
B-1389			48	460	461

752

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1390			44	494	495
B-1391			50	456	457
B-1392			47	451	452
B-1393			44	444	445
B-1394			52	460	461
B-1395			77	440	441
B-1396			58	451	452
B-1397			64	460	461
B-1398			65	504	505
B-1399			50	494	495

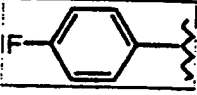
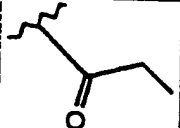
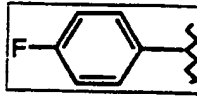
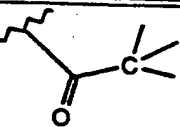
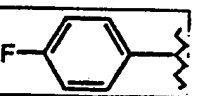
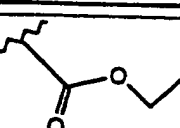
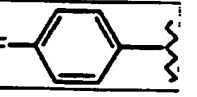
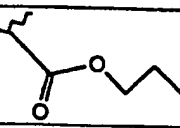
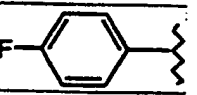
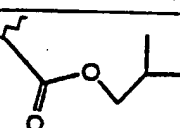
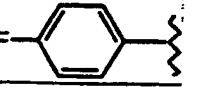
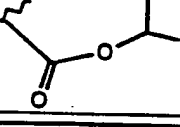
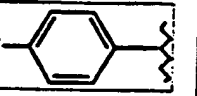
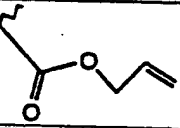
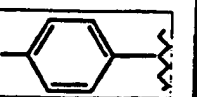
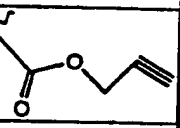
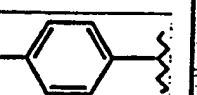
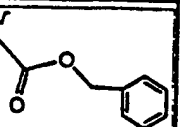
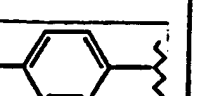
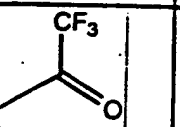
753


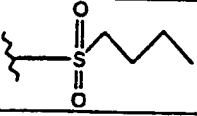
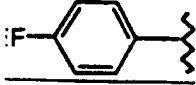
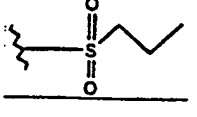
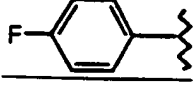
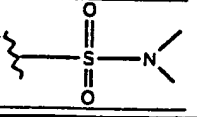
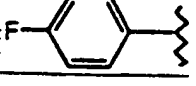
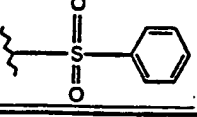
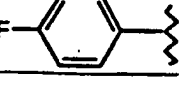
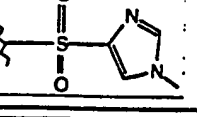
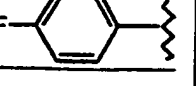
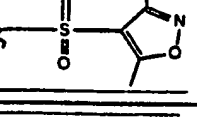
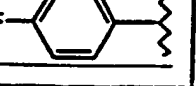
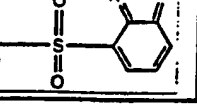
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1400			74	440	441
B-1401			76	462	463
B-1402			65	462	463
B-1403			64	445	446
B-1404			70	512	513
B-1405			57	512	513
B-1406			73	512	513
B-1407			80	512	513
B-1408			2	512	513
B-1409			62	512	513

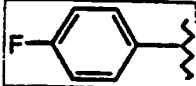
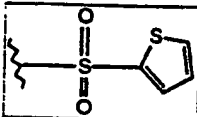
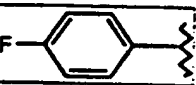
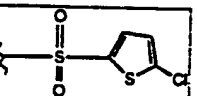
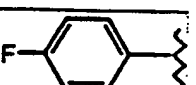
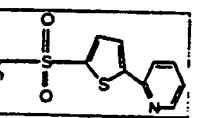
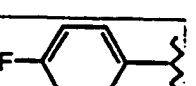
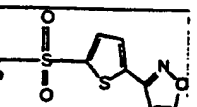
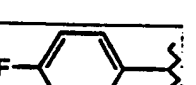
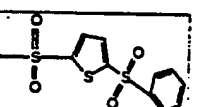
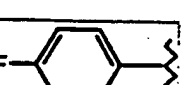
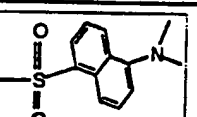
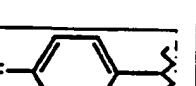
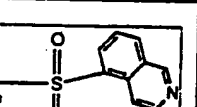
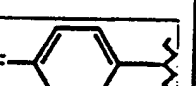
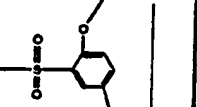
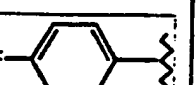
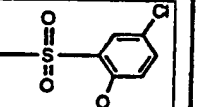
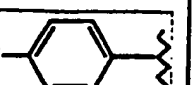
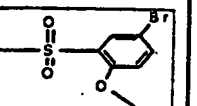
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1410			42	512	513
B-1411			19	462	463
B-1412			74	462	463
B-1413			75	494	495
B-1414			68	462	463
B-1415			48	462	463
B-1416			48	494	495
B-1417			57	494	495
B-1418			49	494	495
B-1419			39	494	495



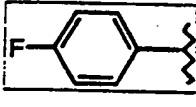
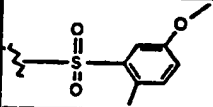
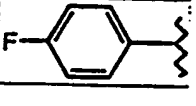
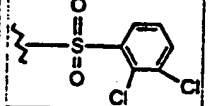
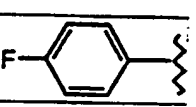
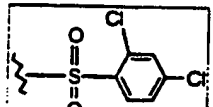
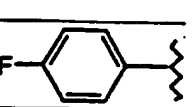
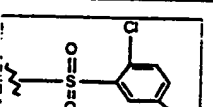
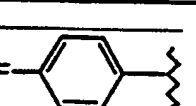
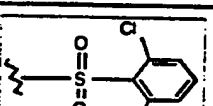
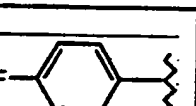
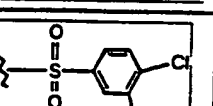
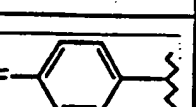
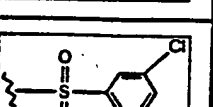
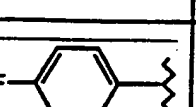
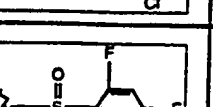
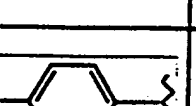
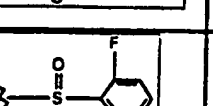

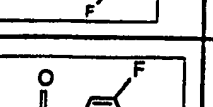
755

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1420			72	378	379
B-1421			74	406	407
B-1422			68	394	395
B-1423			57	408	409
B-1424			77	422	423
B-1425			26	408	409
B-1426			41	406	407
B-1427			37	404	405
B-1428			60	456	457
B-1429			2	418	419


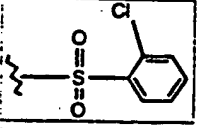
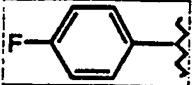
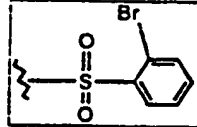
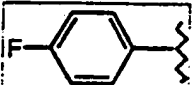
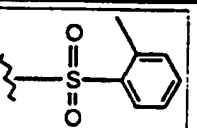
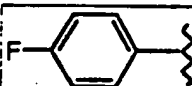
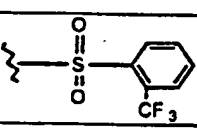
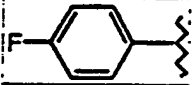
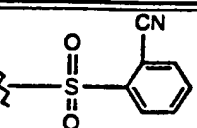
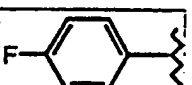
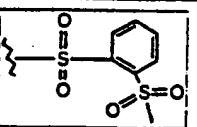
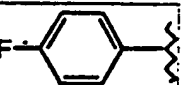
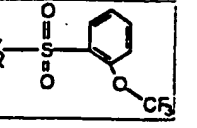
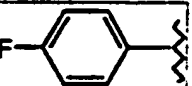
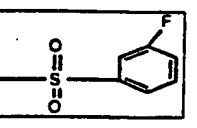
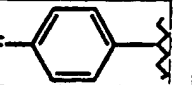
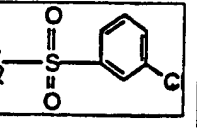
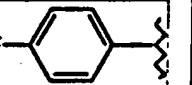
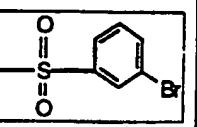
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1430			61	442	443
B-1431			64	428	429
B-1432			71	429	430
B-1433			74	462	463
B-1434			88	466	467
B-1435			75	481	482
B-1436			71	504	505

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1437			63	468	469
B-1438			78	502	503
B-1439			70	545	546
B-1440			62	535	536
B-1441			82	608	
B-1442			79	555	556
B-1443			28	513	514
B-1444			75	522	523
B-1445			74	526	527
B-1446			70	570	571

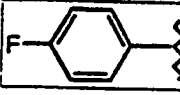
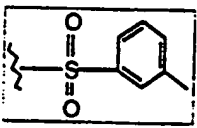
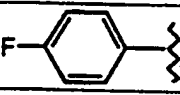
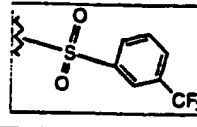
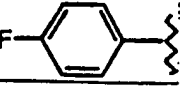
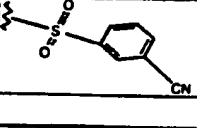
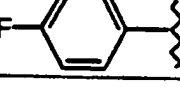
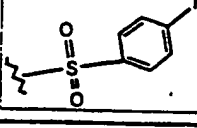
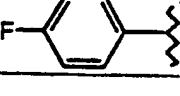
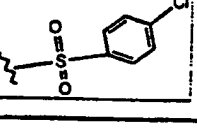
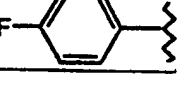
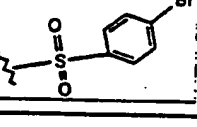
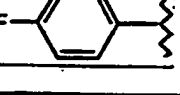
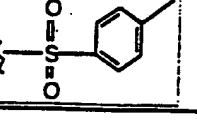
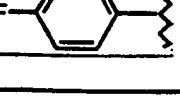
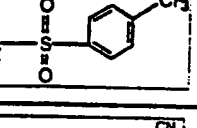

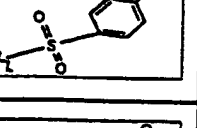

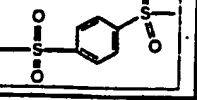
758

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1447			73	506	507
B-1448			76	530	531
B-1449			82	530	531
B-1450			83	530	531
B-1451			74	530	531
B-1452			76	530	531
B-1453			73	530	531
B-1454			81	498	499
B-1455			83	498	499
B-1456			78	498	499

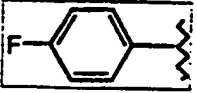

759

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1457			74	496	497
B-1458			82	540	541
B-1459			80	476	477
B-1460			78	530	531
B-1461			82	487	488
B-1462			71	540	541
B-1463			78	546	547
B-1464			83	480	481
B-1465			84	496	497
B-1466			80	540	541

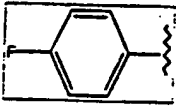
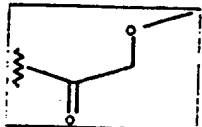

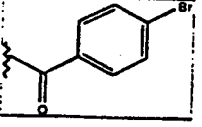
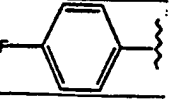
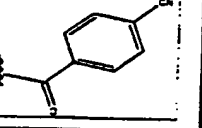
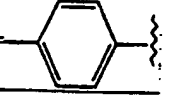
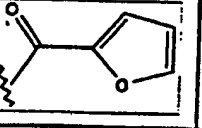
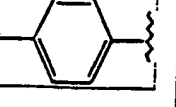
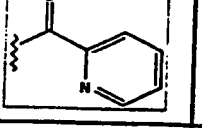
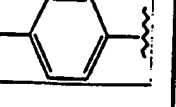
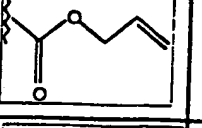
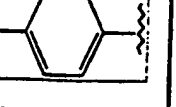
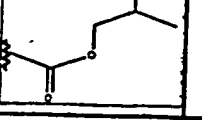
760

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1467			79	476	477
B-1468			79	530	531
B-1469			75	487	488
B-1470			80	480	481
B-1471			74	496	497
B-1472			75	540	541
B-1473			77	476	477
B-1474			81	530	531
B-1475			70	487	488
B-1476			54	540	541

761


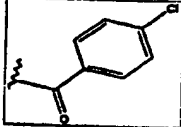
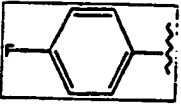
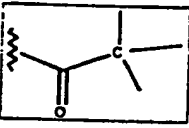

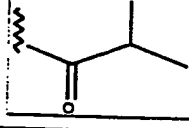
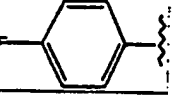
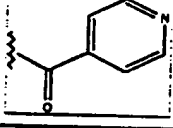
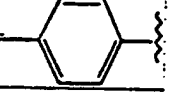
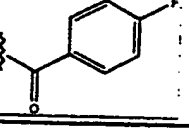
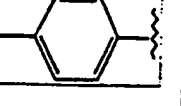
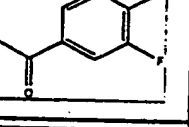
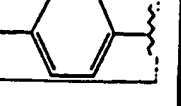
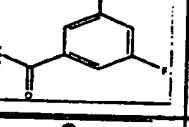
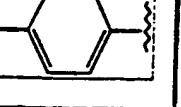


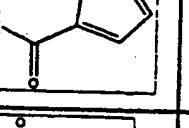
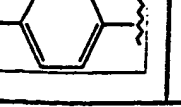
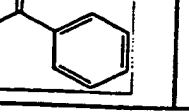
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1477			79	546	547

762


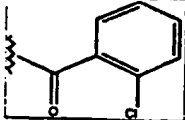
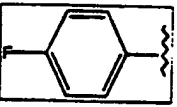
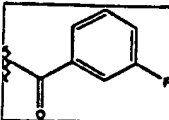
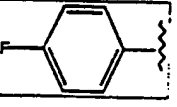
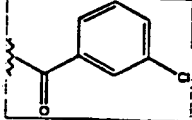


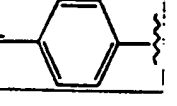
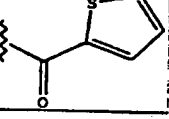
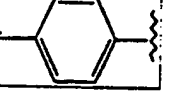
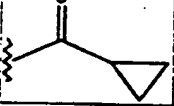
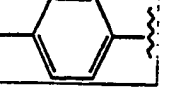
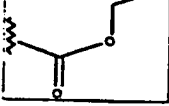
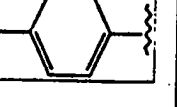
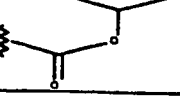
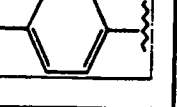
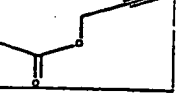
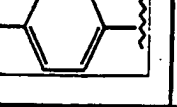
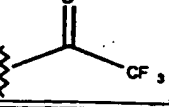
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1478			87	394	395
B-1479			41	504	505
B-1480			87	451	452
B-1481			18	416	417
B-1482			77	427	428
B-1483			74	406	407
B-1484			82	422	423



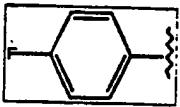
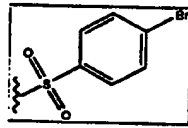
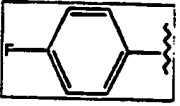
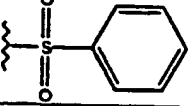
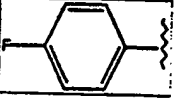
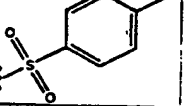
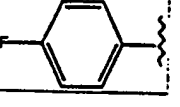
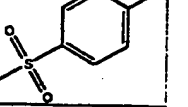
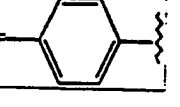
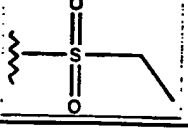
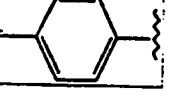
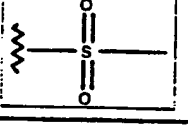
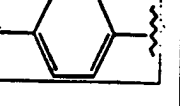
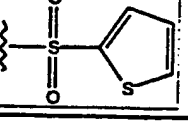
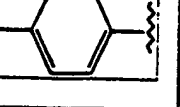
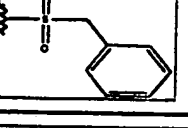

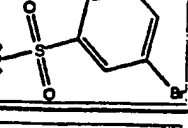

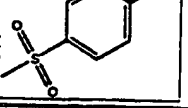
763

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1485			85	460	461
B-1486			64	406	407
B-1487			71	392	393
B-1488			82	427	428
B-1489			87	444	445
B-1490			81	462	463
B-1491			87	462	463
B-1492			69	364	365
B-1493			53	417	418
B-1494			17	426	427

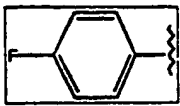
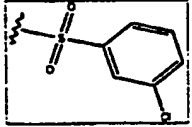

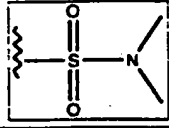
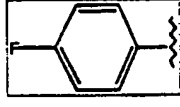
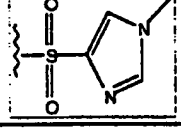
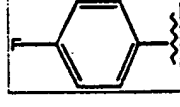
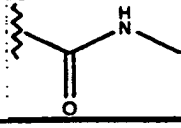

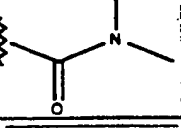
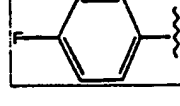
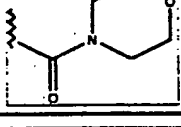
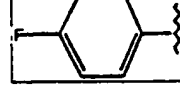
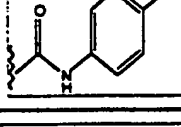
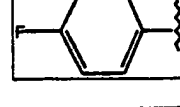
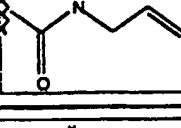
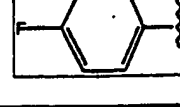
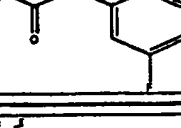
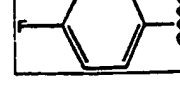
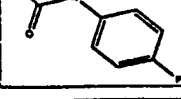
764

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1495			79	460	461
B-1496			80	444	445
B-1497			82	460	461
B-1498			72	378	379
B-1499			70	432	433
B-1500			68	390	391
B-1501			63	394	395
B-1502			78	408	409
B-1503			55	404	405
B-1504			39	418	419

765


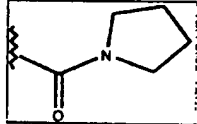
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1505			69	540	541
B-1506			69	462	463
B-1507			70	496	497
B-1508			65	480	481
B-1509			56	414	415
B-1510			62	400	401
B-1511			30	468	469
B-1512			50	476	477
B-1513			44	540	541
B-1514			42	530	531

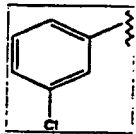
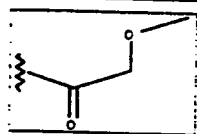
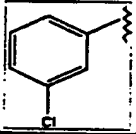
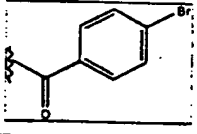
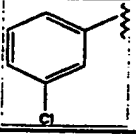
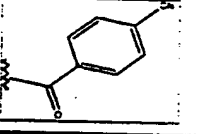
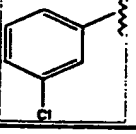
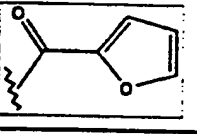
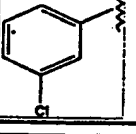
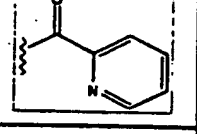
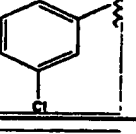
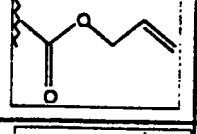
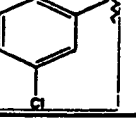
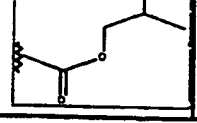
766

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1515			68	496	497
B-1516			27	429	430
B-1517			92	466	467
B-1518			33	379	380
B-1519			50	393	394
B-1520			82	435	436
B-1521			86	509	510
B-1522			12	405	406
B-1523			59	459	460
B-1524			81	459	460

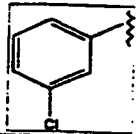
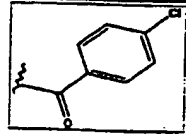
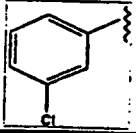
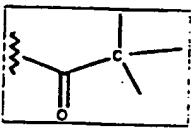
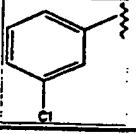
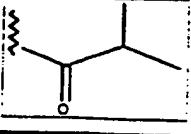
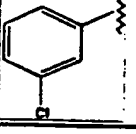
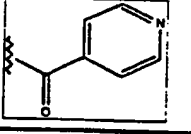
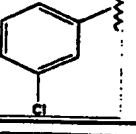
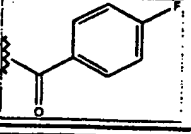
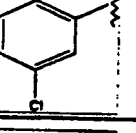
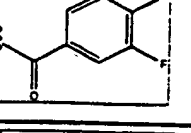
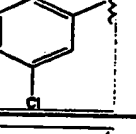
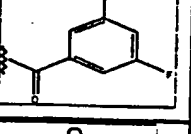
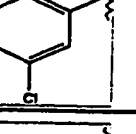
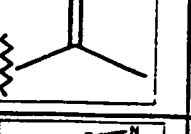
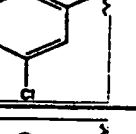
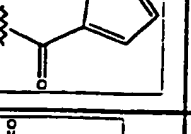
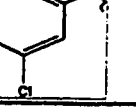
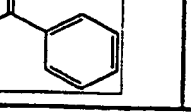
PAGE INTENTIONALLY LEFT BLANK

768

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1525			57	419	420

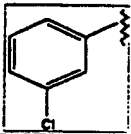
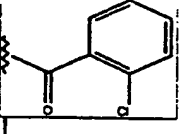
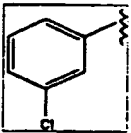
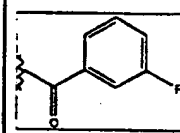
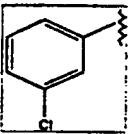
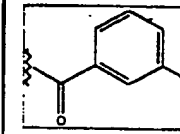
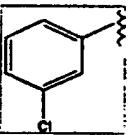
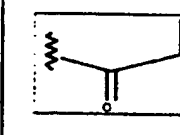
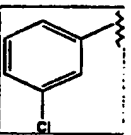
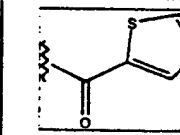
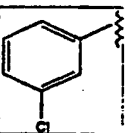
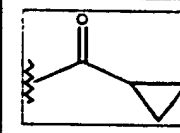
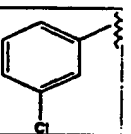
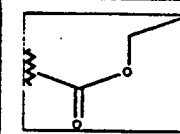
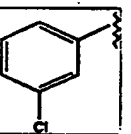
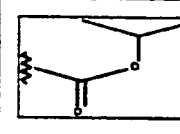
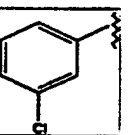
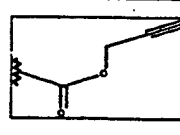
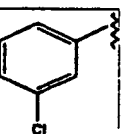
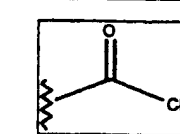
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1526			73	410	411
B-1527			66	520	521
B-1528			91	467	468
B-1529			73	432	433
B-1530			91	443	444
B-1531			74	422	423
B-1532			68	438	439

770

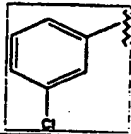
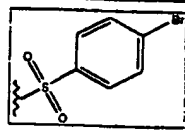
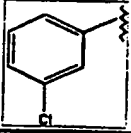
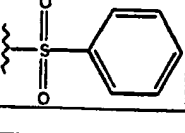
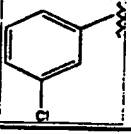
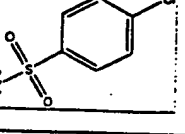
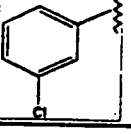
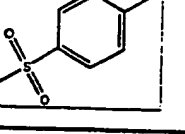
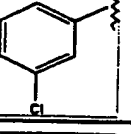
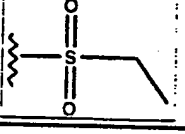
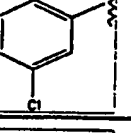
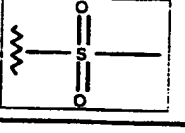
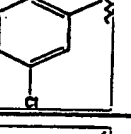
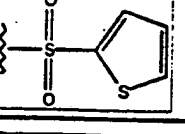
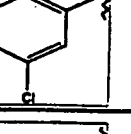
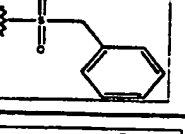
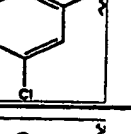
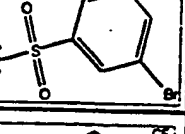
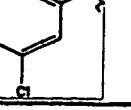
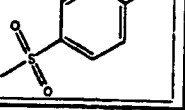
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1533			84	476	477
B-1534			72	422	423
B-1535			78	408	409
B-1536			77	443	444
B-1537			86	460	461
B-1538			74	478	479
B-1539			85	478	479
B-1540			71	380	381
B-1541			71	433	434
B-1542			89	442	443



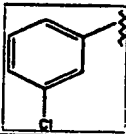
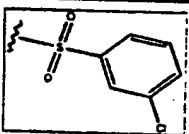
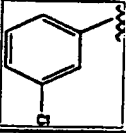
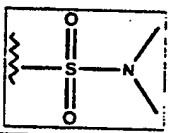
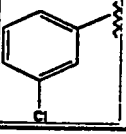
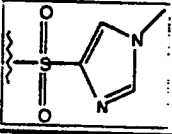
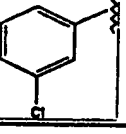
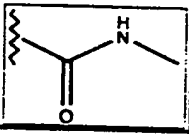
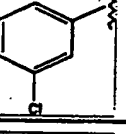
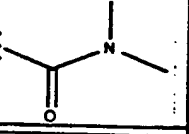
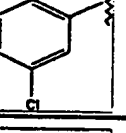
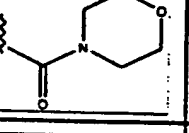
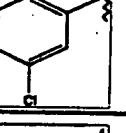
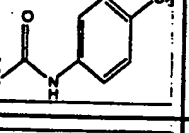
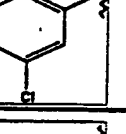
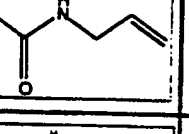
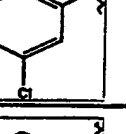
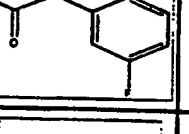

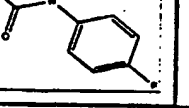
771

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1543			82	476	477
B-1544			76	460	461
B-1545			77	476	477
B-1546			76	394	395
B-1547			58	448	449
B-1548			83	406	407
B-1549			67	410	411
B-1550			37	424	425
B-1551			55	420	421
B-1552			23	434	435

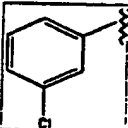
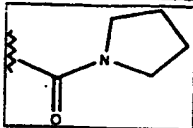
772

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1553			83	556	557
B-1554			84	478	479
B-1555			93	512	513
B-1556			83	496	497
B-1557			62	430	431
B-1558			45	416	417
B-1559			67	484	485
B-1560			16	492	493
B-1561			84	556	557
B-1562			74	546	547

773

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1563			72	512	513
B-1564			57	445	446
B-1565			64	482	483
B-1566			71	395	396
B-1567			54	409	410
B-1568			76	451	452
B-1569			70	525	526
B-1570			79	421	422
B-1571			60	475	476
B-1572			77	475	476

774

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1573			65	435	436

775

5

10

Proton NMR data for selected members from Examples B-0001 through B-1573 are shown in the following table.

15

20

25

30

Plate ID	<sup>1</sup> H NMR(solvent), d ppm
B-0120	(DMF-d7) d 8.53(bd, J = 4.99Hz, 2H), 7.44-7.24(m, 11H), 4.41(s, 2H), 4.31(br, 2H)
B-0224	(DMF-d7) d 8.56(bd, J = 4.98Hz, 2H), 7.78-7.69(m, 4H), 7.39-7.19(m, 6H), 4.23(br, 2H)
B-0235	(DMF-d7) d 8.47(br, 2H), 7.91-7.75(m, 3H), 7.57-7.53(m, 1H), 7.38-7.34(m, 2H), 7.21-7.13(m, 4H), 4.20(br, 2H)
B-0244	(CDCl3/CD3OD) d 8.38(d, J = 5.38 Hz, 1H), 7.62-7.32(m, 9H), 7.04-6.95(m, 4H), 6.86-6.80(m, 2H), 4.52(q, J = 6.96 Hz, 1H), 1.40(d, J = 6.88 Hz, 3H)
B-0256	(DMF-d7) d 8.45(bd, J = 2.85, 2H), 7.87(br s, 4H), 7.76-7.75(m, 2H), 7.53-7.33(m, 5H), 7.18-7.13(br, 4H)
B-0426	(DMF-d7), 1.32(br, 3H), 1.67(br, 3H), 4.17(br, 2H), 5.12(br, 1H), 7.50(m, 6H), 8.77(m, 2H), 13.54(br, 1H).
B-0438	(DMSO), 1.14(t, J = 6.9 Hz, 3H), 4.54(m, 1H), 6.99(br, 2H), 7.21(br, 4H), 7.45(s, 1H), 7.61(q, J = 8.7 Hz, 2H), 8.52(d, J = 5.2 Hz, 2H).
B-0466	(DMF-d7), 1.61(brd, J = 30.6 Hz, 3H), 4.61 (br, 1H), 7.25(m, 6H), 7.65(m, 3H), 8.59(br, 2H), 13.34(brd, J = 34.8 Hz, 1H).
B-0473	(CD3OD), 1.53(d, J = 7.2 Hz, 3H), 4.59(q, J = 7.2 Hz, 1H), 6.88(d, J = 4 Hz, 1H), 7.09(m, 3H), 7.15(dd, J = 4.4, 1.6 Hz, 2H), 7.26(m, 2H), 8.46(d, J = 6.0 Hz, 2H).
B-0477	(DMF), 1.80(br, 3H), 2.35(s, 1H), 4.98(br, 1H), 7.38(m, 6H), 7.85(m, 2H), 8.45(br, 1H), 8.75(d, J = 6.0 Hz, 2H).
B-0479	(Methanol-d4), 1.57(d, J = 5.6 Hz, 3H), 4.74(br, 1H), 7.23(m, 4H), 7.60(m, 2H), 7.81(m, 4H), 8.67(br, 2H).
B-0487	(DMF), 1.78(s, 3H), 2.76(br, 6H), 4.85(br, 1H), 7.42(br, 2H), 7.54(br, 2H), 7.66(br, 3H), 8.82(s, 2H).
B-0566	(CD3OD), 1.38(d, J = 7.2 Hz, 3H), 4.15(br, 2H), 4.50(br, 1H), 7.04(br, 2H), 7.18(br, 2H), 7.30(m, 7H), 8.45(m, 2H).
B-0569	(CD3OD), 1.56(br, 3H), 4.66(q, J = 6.7 Hz, 1H), 7.17(m, 8H), 7.56(m, 2H), 8.47(s, 2H).
B-0574	(Methanol-d4), 1.49(br, 3H), 3.86(br, 3H), 4.60(br, 1H), 6.92(br, 2H), 7.19(br, 2H), 7.31(br, 2H), 7.76(m, 4H), 8.60(br, 2H).
B-0639	(DMF-d7), 1.58(brd, J = 30.0 Hz, 3H), 4.62(br, 1H), 7.25(m, 6H), 7.60(m, 4H), 8.59(br, 2H), 13.30(brd, J = 12.3 Hz).
B-0643	7.18(m, 2H), 7.32(dd, J = 6.0, 4.4 Hz, 1H), 7.70(dd, J = 9.0, 5.8Hz, 1H), 8.43(dd, J = 4.8, 3.2 Hz, 2H).
B-0650	(CD3OD), 1.58(br, 3H), 4.62(q, J = 6.6 Hz, 1H), 6.93(br, 1H), 7.17(m, 5H), 7.31(br, 2H), 8.51(br, 2H).
B-0656	(CDCl3/CD3OD) d 8.48 (d, J = 5.30 Hz, 2H), 7.72-7.59(m, 4H), 7.14-7.10(m, 2H), 7.03-6.97(m, 4H), 4.60(q, J = 7.57Hz, 1H), 1.43(d, J = 7.26Hz, 3H)
B-0663	(CD3OD), 1.52(d, J = 6.8 Hz, 3H), 3.75(s, 3H), 7.21(m, 2H), 7.42(m, 2H), 7.57(s, 1H), 7.76(s, 1H), 7.98(br, 2H), 8.76(br, 2H).
B-1165	Hz, 2H), 3.06(m, 1H), 3.43(q, J = 6.1 Hz, 2H), 7.02(m, 2H), 7.14(m, 2H), 7.41(m, 2H), 8.59(d, J = 5.6 Hz, 2H).
B-1169	= 1.6 Hz, 1H), 7.04(t, J = 8.6 Hz, 2H), 7.14(m, 2H), 7.36(m, 2H), 8.39(d, J = 1.8 Hz, 1H), 8.60(m, 2H).
B-1171	6.83(br, 1H), 7.02(t, J = 8.7 Hz, 2H), 7.15(d, J = 5.6 Hz, 2H), 7.40(m, 2H), 8.59(d, J = 5.0 Hz, 2H).

Plate ID	<sup>1</sup> H NMR(solvent), d ppm
B-1179	(CDCl <sub>3</sub> ), 1.94(br, 2H), 2.53(s, 3H), 2.85(t, J = 6.2 Hz, 2H), 3.65(br, 2H), 6.15(br, 1H), 7.04(m, 3H), 7.22(m, 3H), 7.41(br, 4H), 8.60(br, 2H).
B-1183	(CDCl <sub>3</sub> ), 2.00(br, 2H), 2.85(br, 2H), 3.64(br, 2H), 7.03(br, 3H), 7.17(br, 2H), 7.36(br, 2H), 7.66(br, 2H), 8.60(br, 2H), 8.77(br, 2H).
B-1194	(DMSO), 1.76(br, 2H), 2.66(br, 2H), 2.91(br, 2H), 4.30(s, 2H), 7.18(br, 5H), 7.35(m, 6H), 8.54(d, J = 5.8 Hz, 2H).
B-1200	(DMSO), 1.17(br, 3H), 1.76(br, 2H), 2.71(br, 2H), 2.97(br, 4H), 7.18(br, 4H), 7.36(br, 2H), 8.54(br, 2H).
B-1206	(DMSO), 1.03(s, 6H), 1.68(br, 2H), 2.63(br, 2H), 3.00(br, 2H), 3.65(br, 1H), 5.69(m, 2H), 7.16(br, 4H), 7.35(br, 2H), 8.54(br, 2H).
B-1216	(DMSO), 1.75(m, 2H), 2.14(s, 6H), 2.66(br, 2H), 3.10(br, 2H), 7.04(br, 3H), 7.18(br, 4H), 7.35(m, 2H), 7.47(br, 1H), 8.54(d, J = 4.8 Hz, 2H).
B-1226	(DMF), 1.25(br, 3H), 2.01(br, 2H), 3.35(br, 4H), 6.20(s, 1H), 6.30(s, 1H), 7.42(br, 4H), 7.65(br, 2H), 8.77(s, 2H).
B-1360	(DMSO-d <sub>6</sub> ), 1.80(br, 4H), 2.82(br, 1H), 2.94(br, 1H), 3.10(br, 1H), 3.60(br, 1H), 4.54(br, 1H), 7.18(m, 4H), 7.30(m, 4H), 7.46(m, 2H), 8.54(br, 2H).
B-1361	(DMSO-d <sub>6</sub> ), 0.99(br, 6H), 1.73(br, 4H), 2.89(br, 2H), 3.03(m, 1H), 4.04(br, 2H), 4.44(m, 1H), 7.18(m, 4H), 7.30(m, 2H), 8.57(d, J = 4.64 Hz, 2H).
B-1363	(DMSO-d <sub>6</sub> ), 1.78(br, 4H), 2.01(s, 3H), 2.89(br, 1H), 3.05(br, 1H), 3.34(br, 1H), 3.85(br, 1H), 4.48(br, 1H), 7.12(br, 2H), 7.21(br, 2H), 7.30(br, 2H), 8.69(br, 2H).
B-1364	(CDCl <sub>3</sub> ), 0.78(dd, J = 3.0, 2.9 Hz, 2H), 1.00(s, 2H), 1.78(m, 1H), 1.86(b, 4H), 2.64(m, 1H), 2.99(m, 1H), 3.16(m, 1H), 4.33(br, 1H), 4.70(br, 1H), 6.99(m, 2H), 7.14(s, 2H), 7.29(m, 2H), 8.64(s, 2H).
B-1368	(CDCl <sub>3</sub> ), 1.89(s, 4H), 2.65(m, 1H), 2.96(m, 1H), 3.06(m, 1H), 3.43(s, 3H), 3.93(d, J = 13.2 Hz, 1H), 4.09(d, J = 13.5 Hz, 1H), 4.18(d, J = 13.5 Hz, 1H), 4.68(d, J = 12.4 Hz, 1H), 7.60(m, 2H), 7.12(s, 2H), 7.26(m, 2H), 8.63(s, 2H).

778

5

10

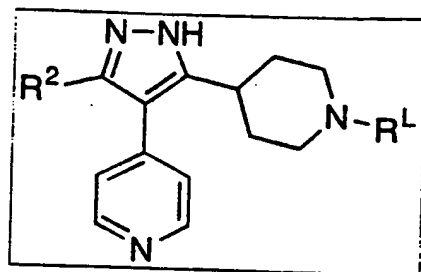
By analogy to the procedure identified above for the  
preparation of Examples B0001-B0048, the following  
15 examples B-1574 through B-2269 are prepared.

20

25

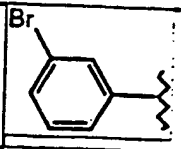
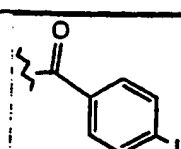
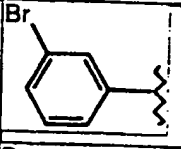
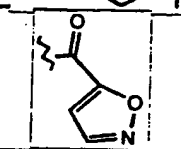
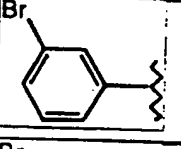
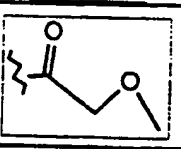
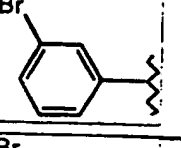
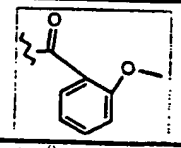
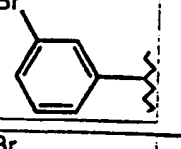
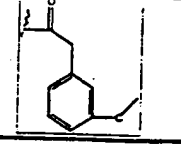
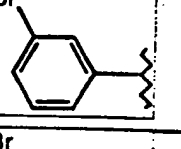
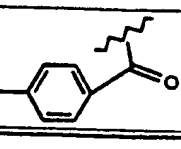
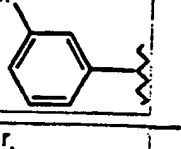
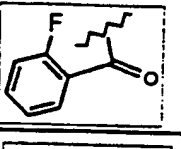
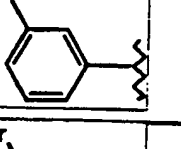
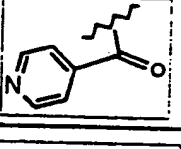
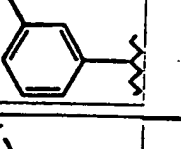
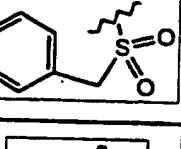

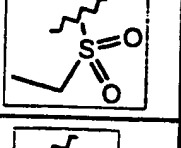
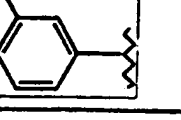
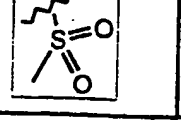
30



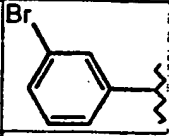
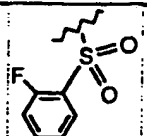
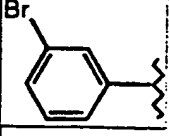
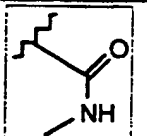
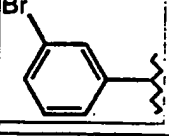
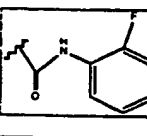
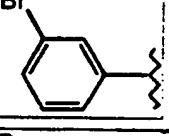
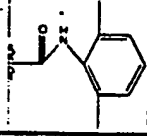
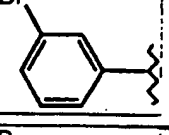
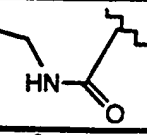
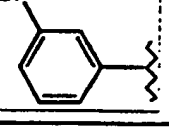
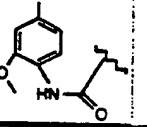


Examples B-1574 through B-1597 are prepared from Scaffold C-27

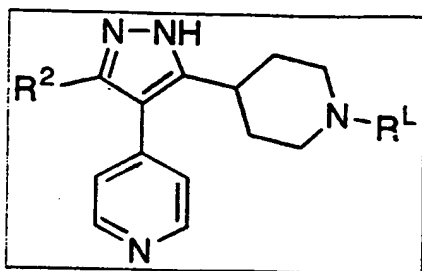
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1574					
B-1575					
B-1576					
B-1577					
B-1578					
B-1579					
B-1580					

B-1581					
B-1582					
B-1583					
B-1584					
B-1585					
B-1586					
B-1587					
B-1588					
B-1589					
B-1590					
B-1591					

781

B-1592					
B-1593					
B-1594					
B-1595					
B-1596					
B-1597					

782



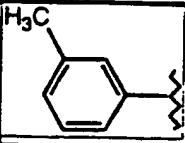
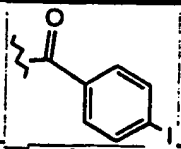
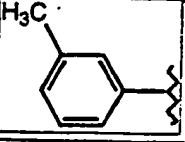
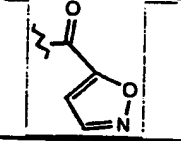
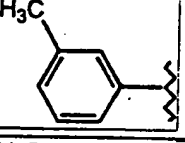
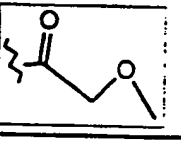
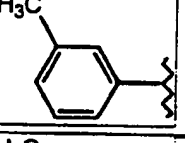
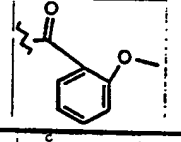
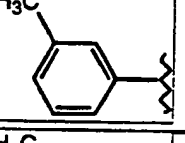
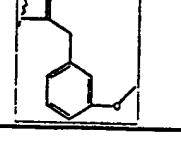
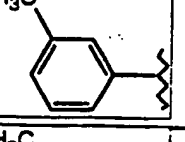
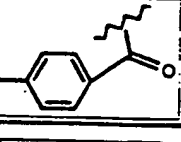
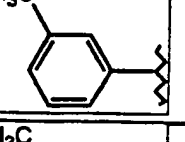
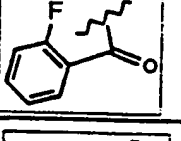
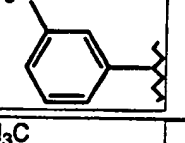
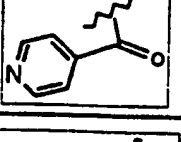
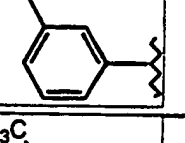
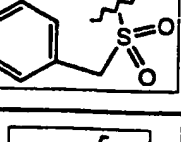
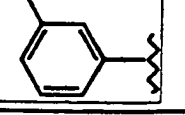
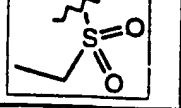
Examples B-1598 through B-1621 are prepared from Scaffold C-28

Example#

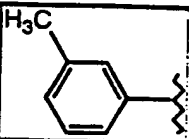
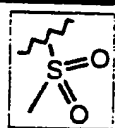
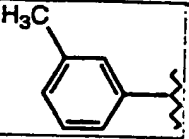
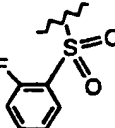
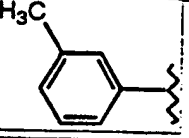
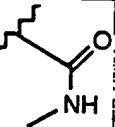
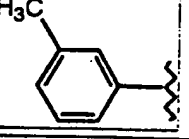
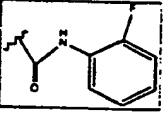
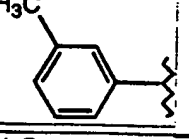
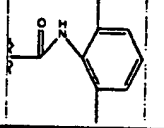
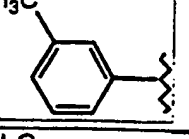
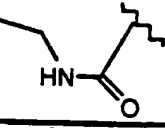
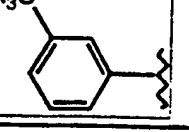
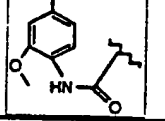
 $R^2$  $R^L$ 

B-1598					
B-1599					
B-1600					
B-1601					
B-1602					
B-1603					
B-1604					

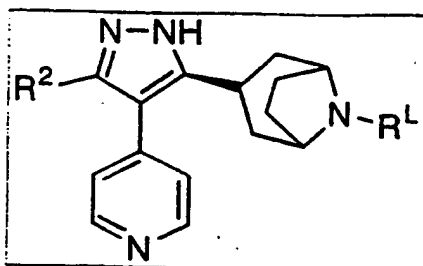
783

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1605					
B-1606					
B-1607					
B-1608					
B-1609					
B-1610					
B-1611					
B-1612					
B-1613					
B-1614					

784

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1615					
B-1616					
B-1617					
B-1618					
B-1619					
B-1620					
B-1621					

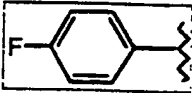
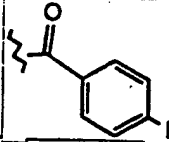
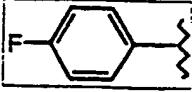
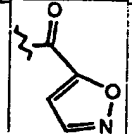
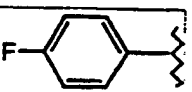
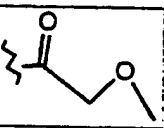
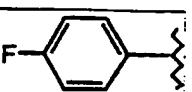
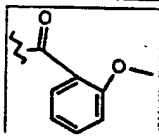
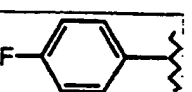
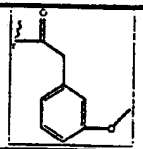
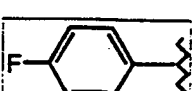
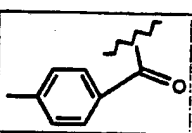
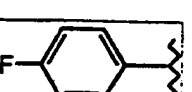
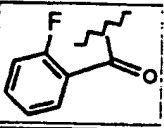
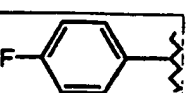
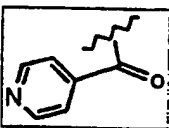
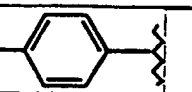
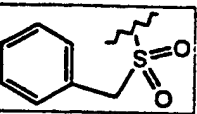
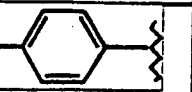
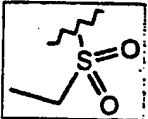
785



Examples B-1622 through B-1645 are prepared from Scaffold C-38

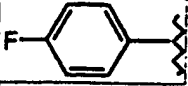
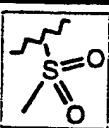
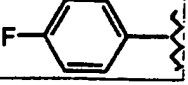
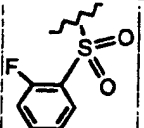
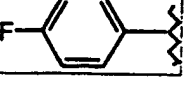
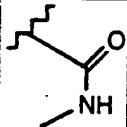
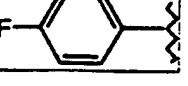
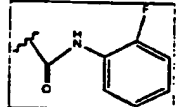
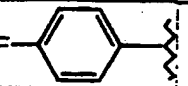
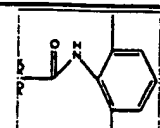
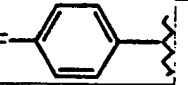
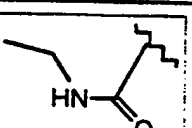
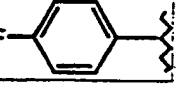
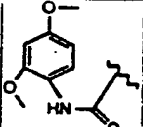
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1622					
B-1623					
B-1624					
B-1625					
B-1626					
B-1627					
B-1628					

786

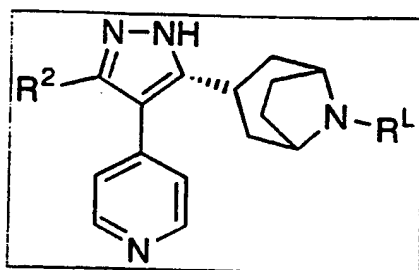
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1629					
B-1630					
B-1631					
B-1632					
B-1633					
B-1634					
B-1635					
B-1636					
B-1637					
B-1638					



787

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1639					
B-1640					
B-1641					
B-1642					
B-1643					
B-1644					
B-1645					

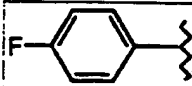
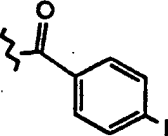

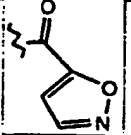
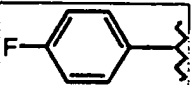
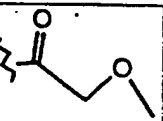
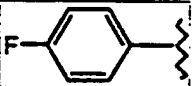
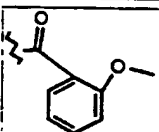
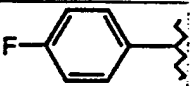
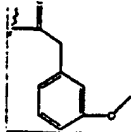
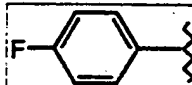
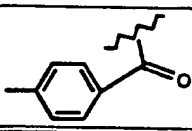
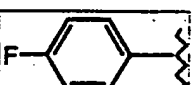
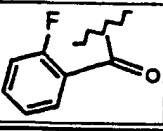
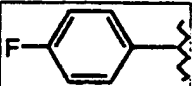
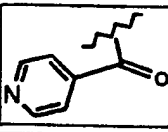
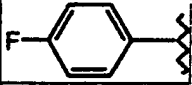
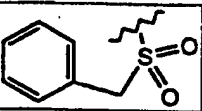
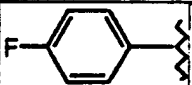
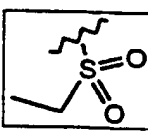
788

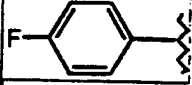
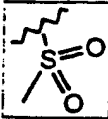
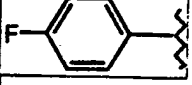
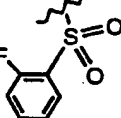
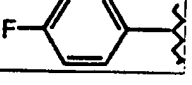
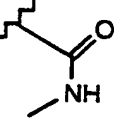
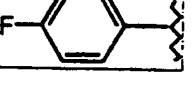
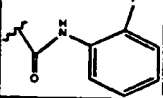
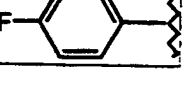
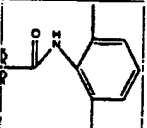
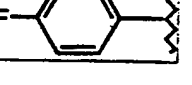
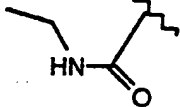

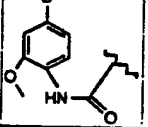


Examples B-1646 through B-1669 are prepared from Scaffold C-39

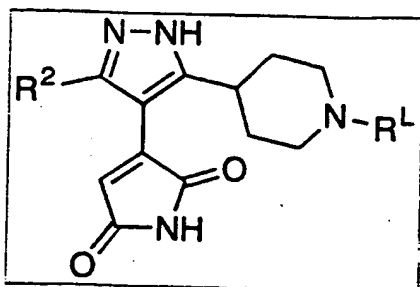
Example#	R²	R¹			
B-1646					
B-1647					
B-1648					
B-1649					
B-1650					
B-1651					
B-1652					

789

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1653					
B-1654					
B-1655					
B-1656					
B-1657					
B-1658					
B-1659					
B-1660					
B-1661					
B-1662					

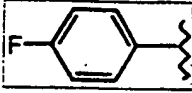
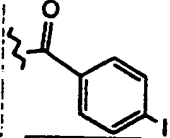
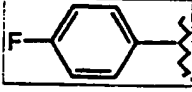
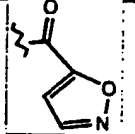
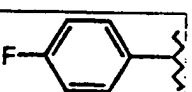
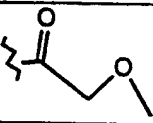
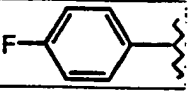
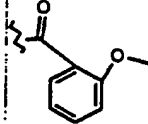
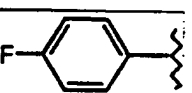
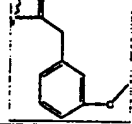
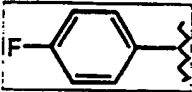
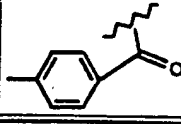
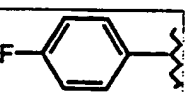
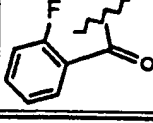
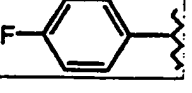
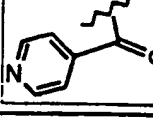
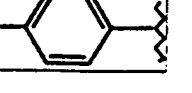
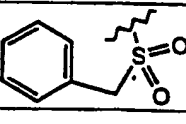
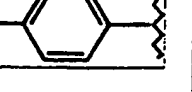
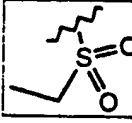
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1663					
B-1664					
B-1665					
B-1666					
B-1667					
B-1668					
B-1669					

791

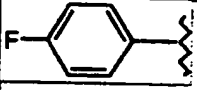
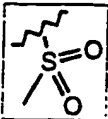
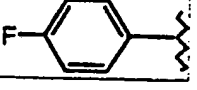
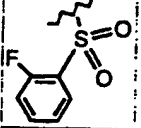
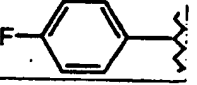
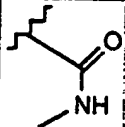
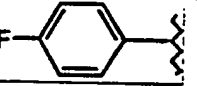
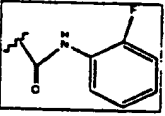
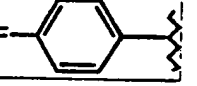
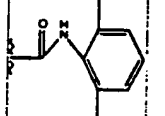
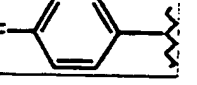
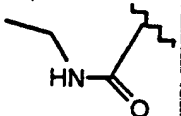
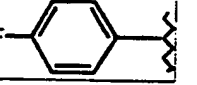
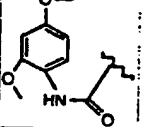


Examples B-1670 through B-1693 are prepared from Scaffold C-65

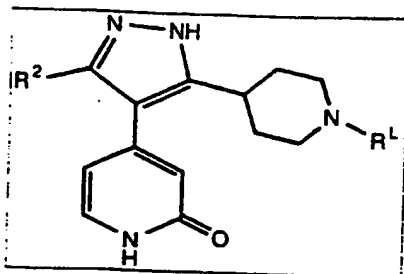
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1670					
B-1671					
B-1672					
B-1673					
B-1674					
B-1675					
B-1676					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1677					
B-1678					
B-1679					
B-1680					
B-1681					
B-1682					
B-1683					
B-1684					
B-1685					
B-1686					

793

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1687					
B-1688					
B-1689					
B-1690					
B-1691					
B-1692					
B-1693					

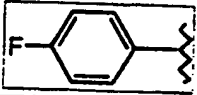
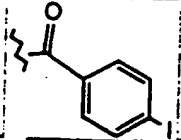
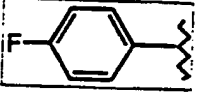
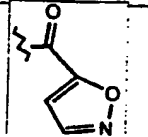
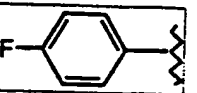
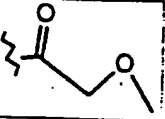
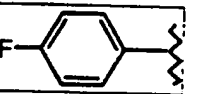
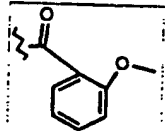
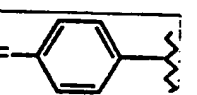
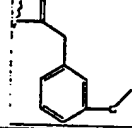
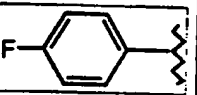
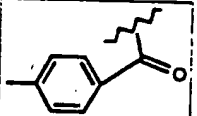
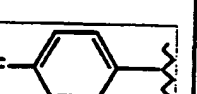
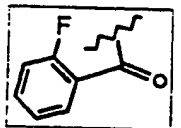
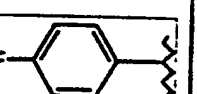
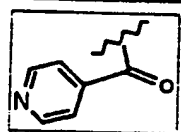
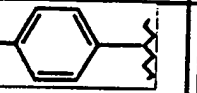
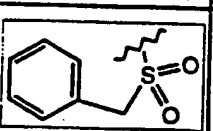
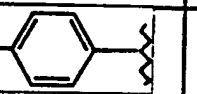
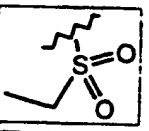
794



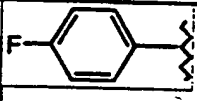
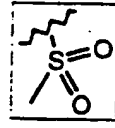
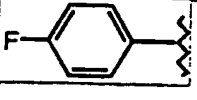
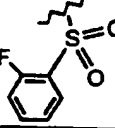
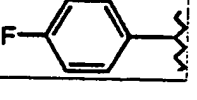
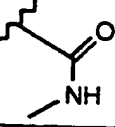
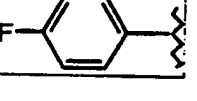
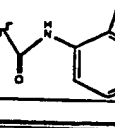
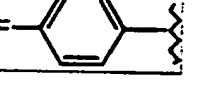
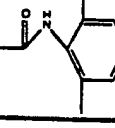
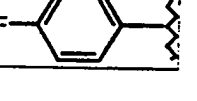
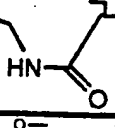
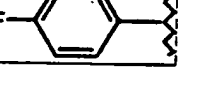
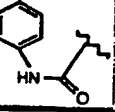
Examples B-1694 through B-1717 are prepared from Scaffold C-66

Example#	$R^2$	$R^1$			
B-1694					
B-1695					
B-1696					
B-1697					
B-1698					
B-1699					
B-1700					

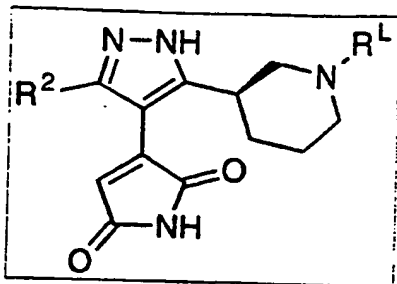


Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1701					
B-1702					
B-1703					
B-1704					
B-1705					
B-1706					
B-1707					
B-1708					
B-1709					
B-1710					

796

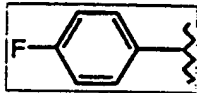
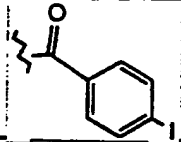
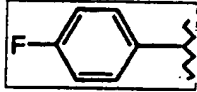
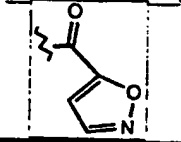
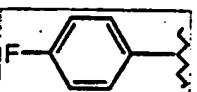
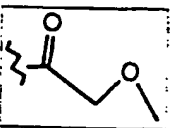
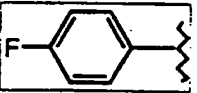
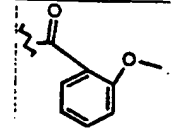
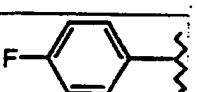
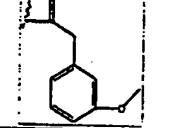
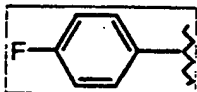
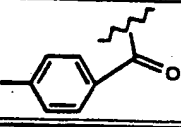
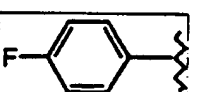
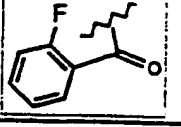
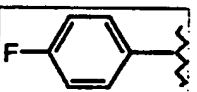
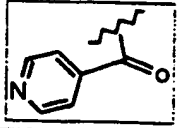
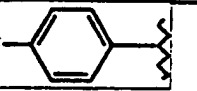
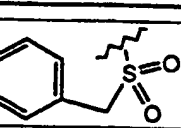
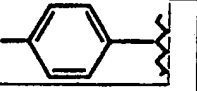
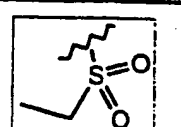
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1711					
B-1712					
B-1713					
B-1714					
B-1715					
B-1716					
B-1717					

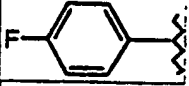
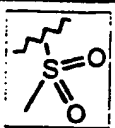
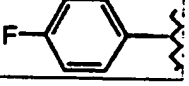
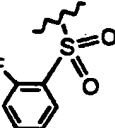
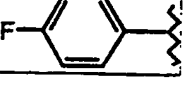
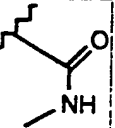
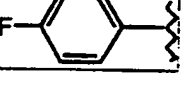
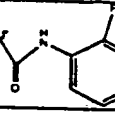
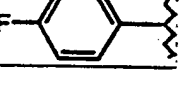
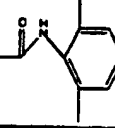

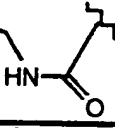
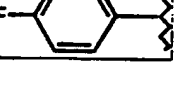
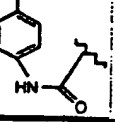
797



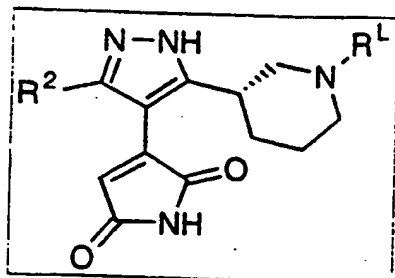
Examples B-1718 through B-1741 are prepared from Scaffold C-69

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1718					
B-1719					
B-1720					
B-1721					
B-1722					
B-1723					
B-1724					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1725					
B-1726					
B-1727					
B-1728					
B-1729					
B-1730					
B-1731					
B-1732					
B-1733					
B-1734					

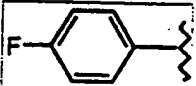
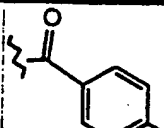
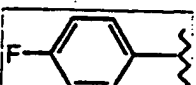
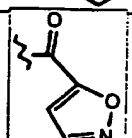
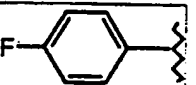
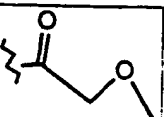
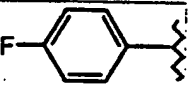
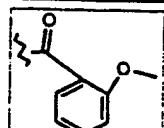
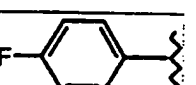
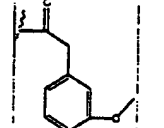
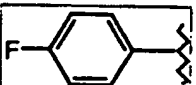
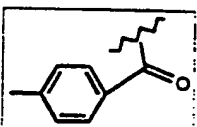
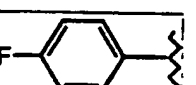
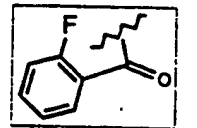
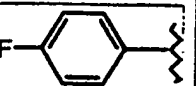
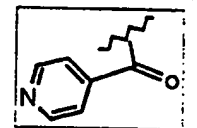
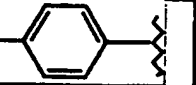
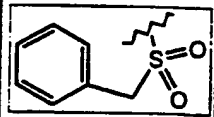
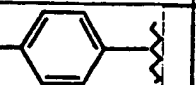
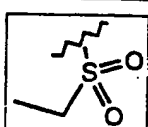
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1735					
B-1736					
B-1737					
B-1738					
B-1739					
B-1740					
B-1741					

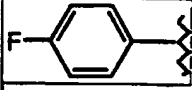
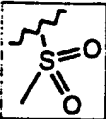
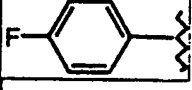
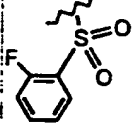
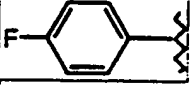
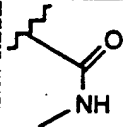
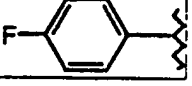
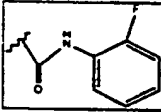
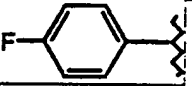
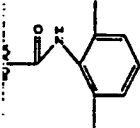
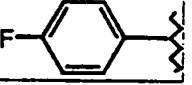
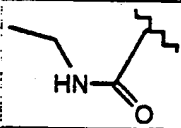
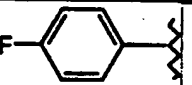
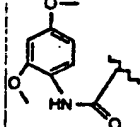
800



Examples B-1742 through B-1765 are prepared from Scaffold C-70

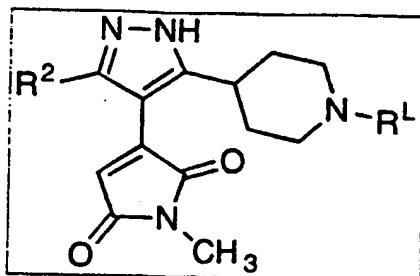
Example#	R <sup>2</sup>	R <sup>4</sup>			
B-1742					
B-1743					
B-1744					
B-1745					
B-1746					
B-1747					
B-1748					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1749					
B-1750					
B-1751					
B-1752					
B-1753					
B-1754					
B-1755					
B-1756					
B-1757					
B-1758					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1759					
B-1760					
B-1761					
B-1762					
B-1763					
B-1764					
B-1765					

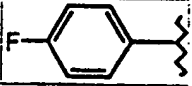
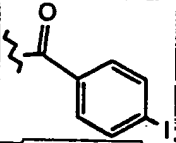
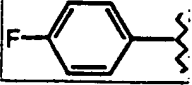
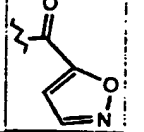
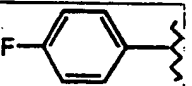
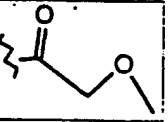
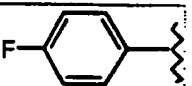
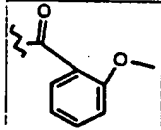
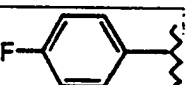
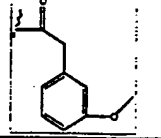
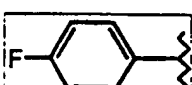
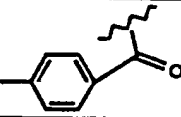
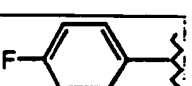
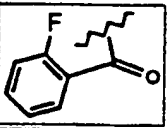
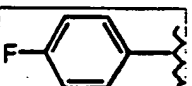
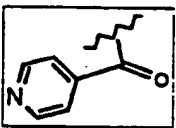
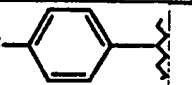
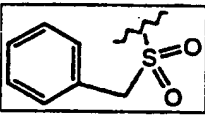
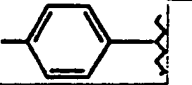
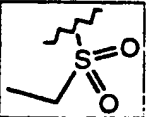


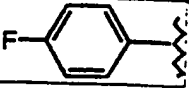
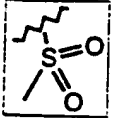
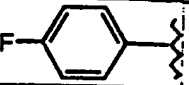
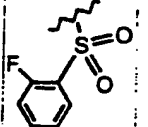
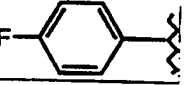
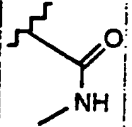
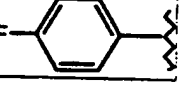
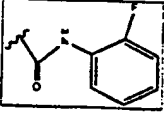
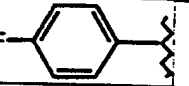
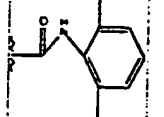
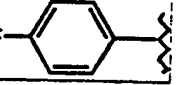
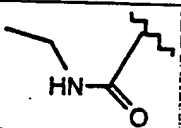
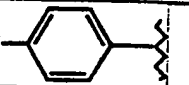
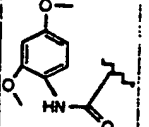
803



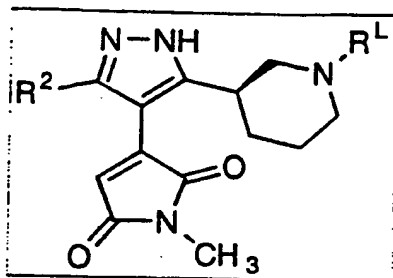
Examples B-1766 through B-1789 are prepared from Scaffold C-71

Example#	$R^2$	$R^L$			
B-1766					
B-1767					
B-1768					
B-1769					
B-1770					
B-1771					
B-1772					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1773					
B-1774					
B-1775					
B-1776					
B-1777					
B-1778					
B-1779					
B-1780					
B-1781					
B-1782					

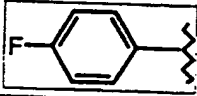
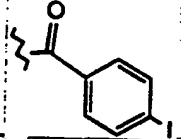
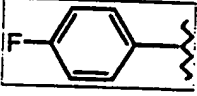
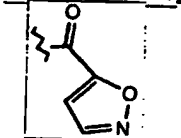
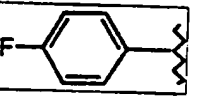
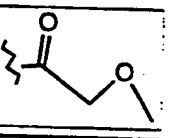
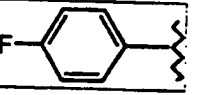
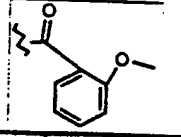
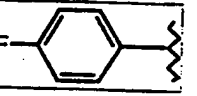
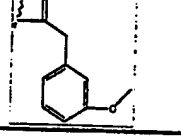
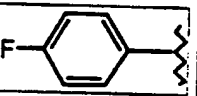
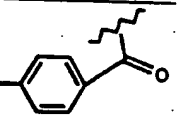
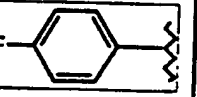
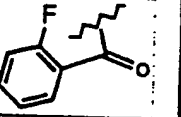
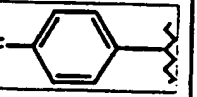
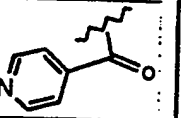
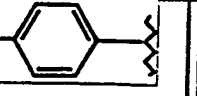
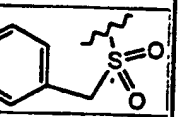
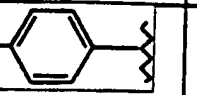
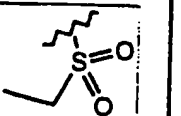
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1783					
B-1784					
B-1785					
B-1786					
B-1787					
B-1788					
B-1789					

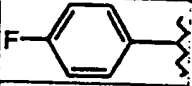
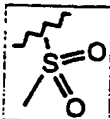
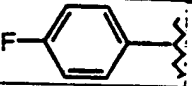
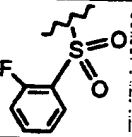
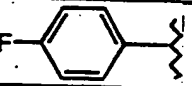
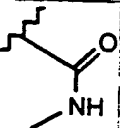
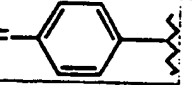
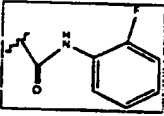
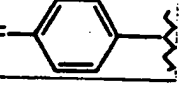
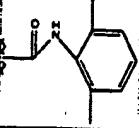
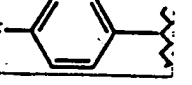
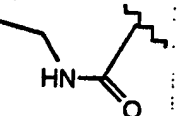
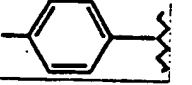
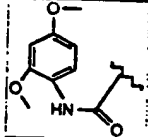
806

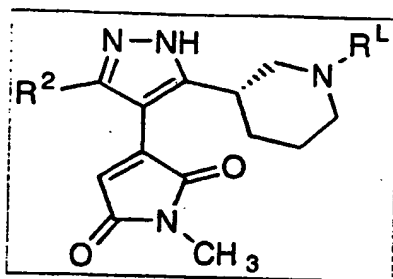


Examples B-1790 through B-1813 are prepared from Scaffold C-72

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1790					
B-1791					
B-1792					
B-1793					
B-1794					
B-1795					
B-1796					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1797					
B-1798					
B-1799					
B-1800					
B-1801					
B-1802					
B-1803					
B-1804					
B-1805					
B-1806					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1807					
B-1808					
B-1809					
B-1810					
B-1811					
B-1812					
B-1813					

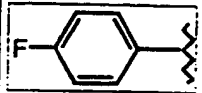
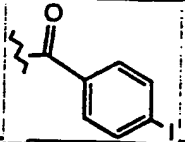
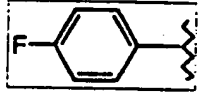
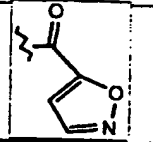
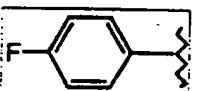
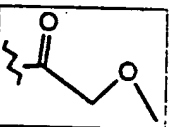
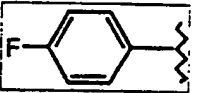
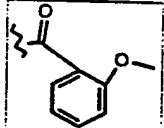
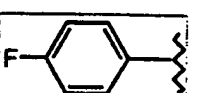
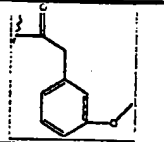
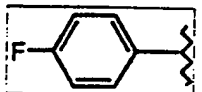
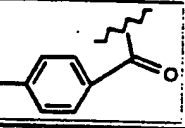
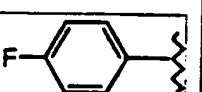
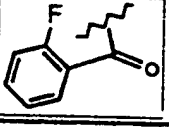
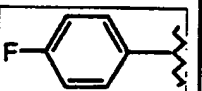
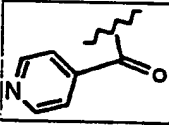
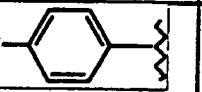
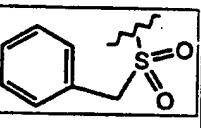
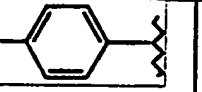
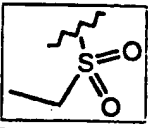


Examples B-1814 through B-1837 are prepared from Scaffold C-73

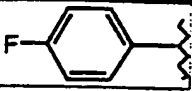
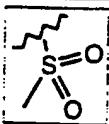
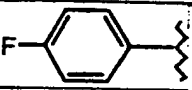
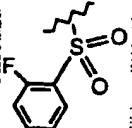
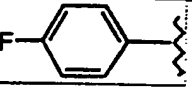
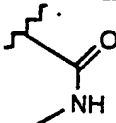
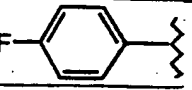
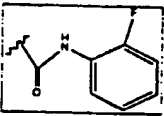
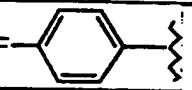
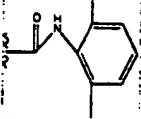
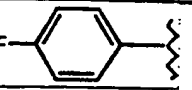
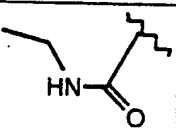
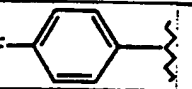
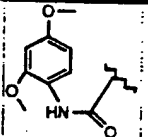
Example#	R <sup>2</sup>	R <sup>4</sup>			
B-1814					
B-1815					
B-1816					
B-1817					
B-1818					
B-1819					
B-1820					

Example#

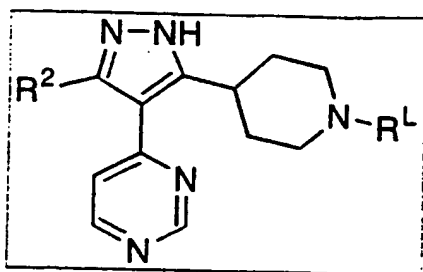
 $R^2$  $R^1$ 

B-1821					
B-1822					
B-1823					
B-1824					
B-1825					
B-1826					
B-1827					
B-1828					
B-1829					
B-1830					



Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1831					
B-1832					
B-1833					
B-1834					
B-1835					
B-1836					
B-1837					

812

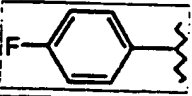
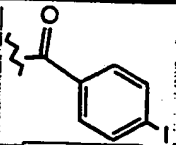
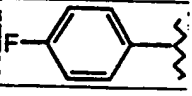
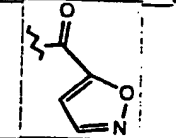
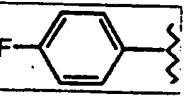
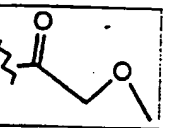
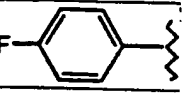
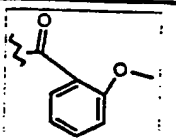
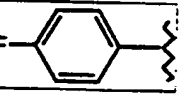
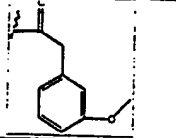
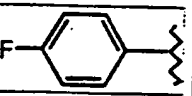
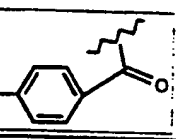
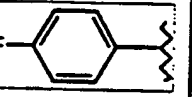
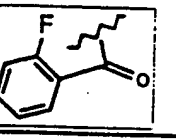
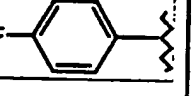
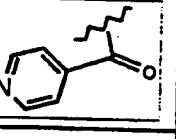
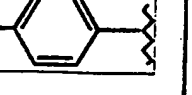
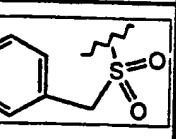
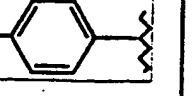
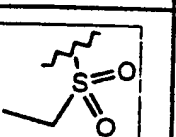


Examples B-1838 through B-1861 are prepared from Scaffold C-33

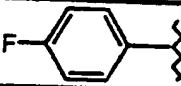
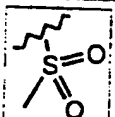
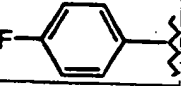
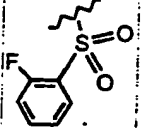
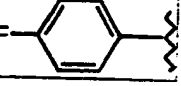
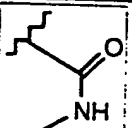
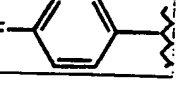
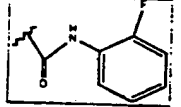
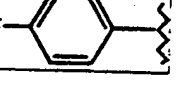
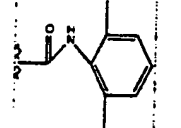
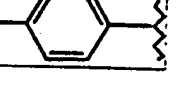
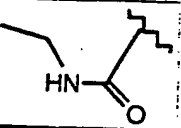
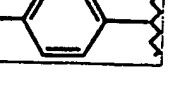
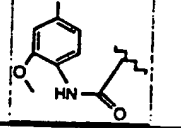
Example#

 $R^2$  $R^1$ 

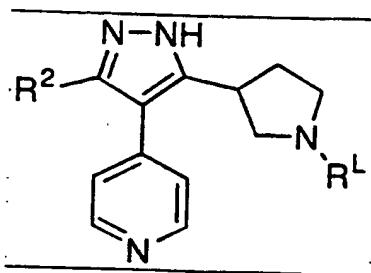
B-1838					
B-1839					
B-1840					
B-1841					
B-1842					
B-1843					
B-1844					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1845					
B-1846					
B-1847					
B-1848					
B-1849					
B-1850					
B-1851					
B-1852					
B-1853					
B-1854					

814

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1855					
B-1856					
B-1857					
B-1858					
B-1859					
B-1860					
B-1861					

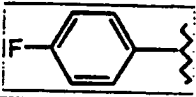
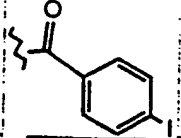
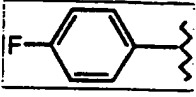
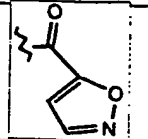
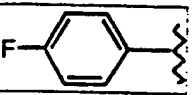
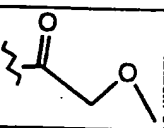
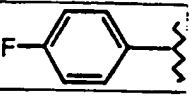
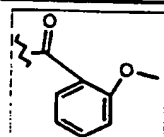
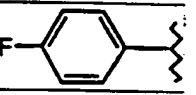
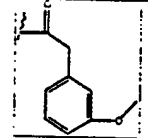
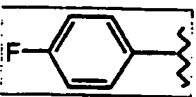
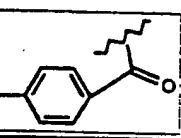
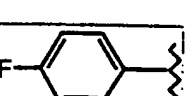
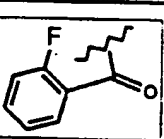
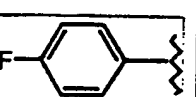
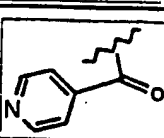
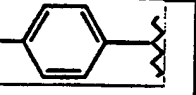
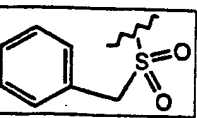
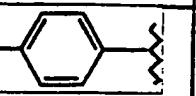
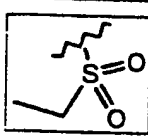
815

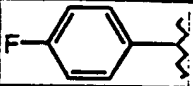
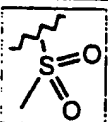
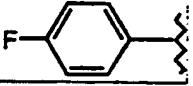
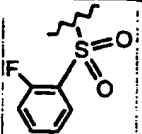
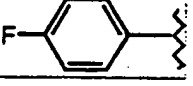
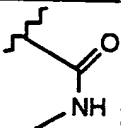
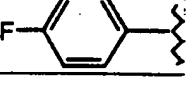
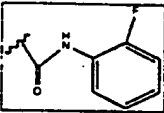
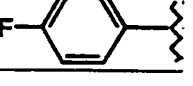
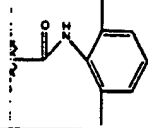
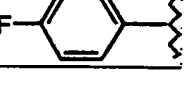
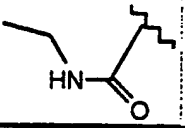
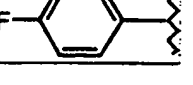
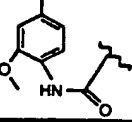


Examples B-1862 through B-1885 are prepared from Scaffold C-45

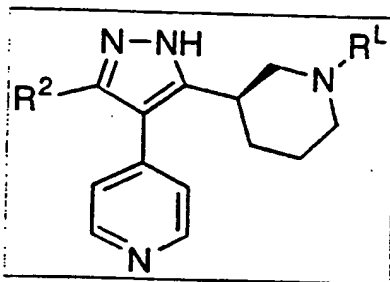
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1862					
B-1863					
B-1864					
B-1865					
B-1866					
B-1867					
B-1868					

816

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1869					
B-1870					
B-1871					
B-1872					
B-1873					
B-1874					
B-1875					
B-1876					
B-1877					
B-1878					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1879					
B-1880					
B-1881					
B-1882					
B-1883					
B-1884					
B-1885					

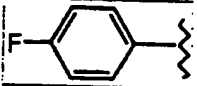
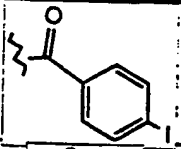

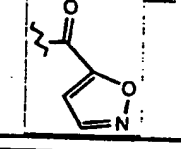
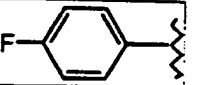
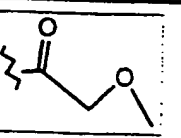
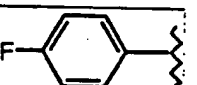
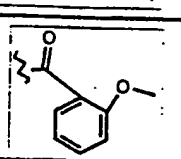
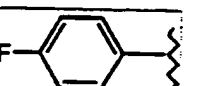
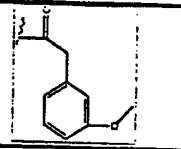
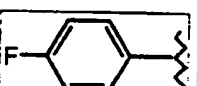
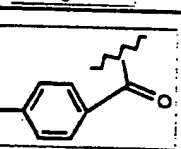
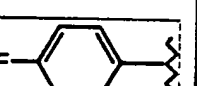
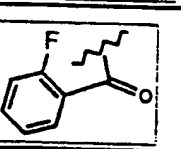
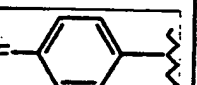
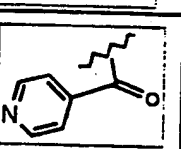
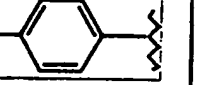
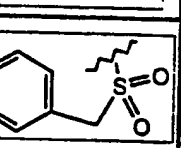
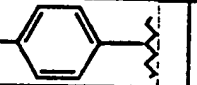
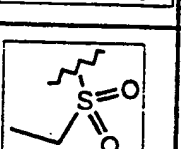
818

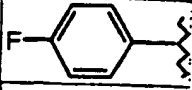
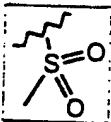
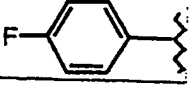
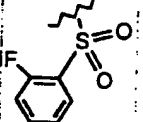
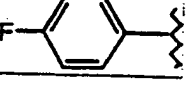
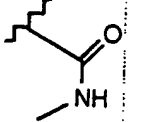
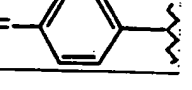
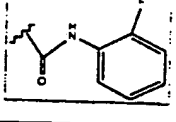
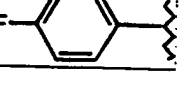
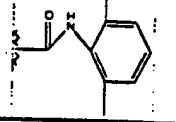
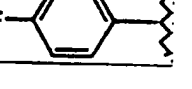
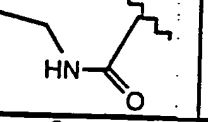
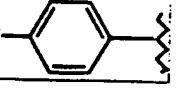
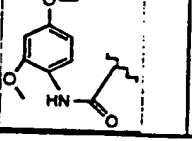


Examples B-1886 through B-1909 prepared from Scaffold C-42

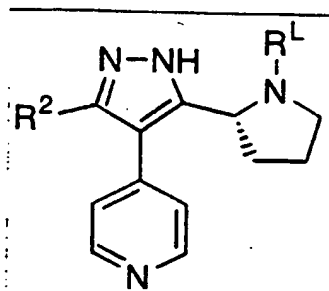
Example#	$R^2$	$R^4$			
B-1886					
B-1887					
B-1888					
B-1889					
B-1890					
B-1891					
B-1892					



Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1893					
B-1894					
B-1895					
B-1896					
B-1897					
B-1898					
B-1899					
B-1900					
B-1901					
B-1902					

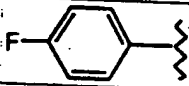
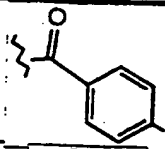
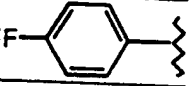
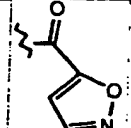
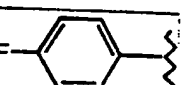
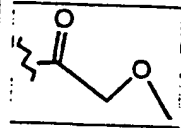
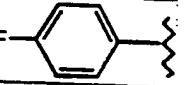
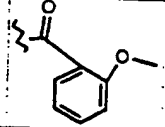
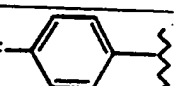
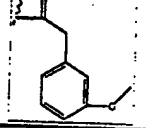
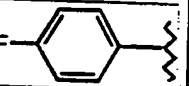
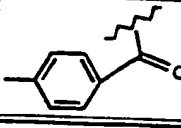
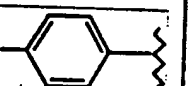
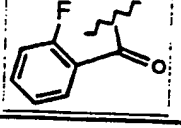
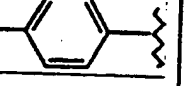
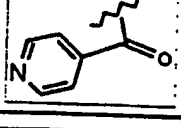
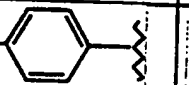
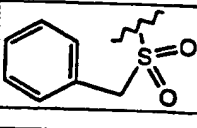
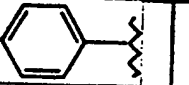
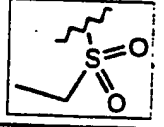
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1903					
B-1904					
B-1905					
B-1906					
B-1907					
B-1908					
B-1909					

821

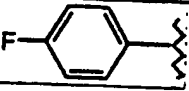
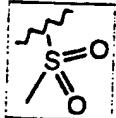
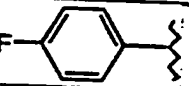
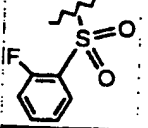
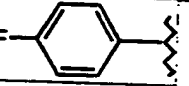
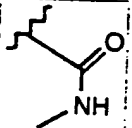
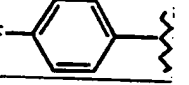
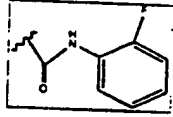
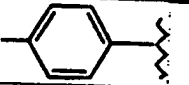
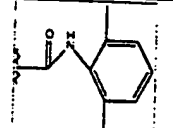
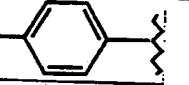
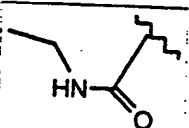
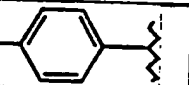
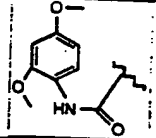


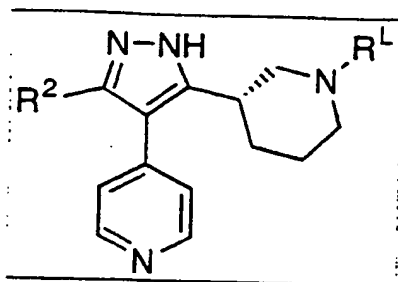
Examples B-1910 through B-1933 are prepared from Scaffold C-44

Example#	$R^2$	$R^L$			
B-1910					
B-1911					
B-1912					
B-1913					
B-1914					
B-1915					
B-1916					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1917					
B-1918					
B-1919					
B-1920					
B-1921					
B-1922					
B-1923					
B-1924					
B-1925					
B-1926					

823

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1927					
B-1928					
B-1929					
B-1930					
B-1931					
B-1932					
B-1933					


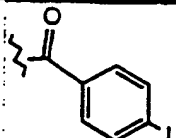

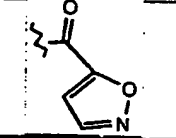
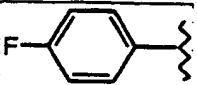
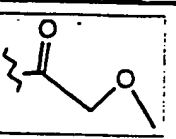
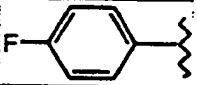
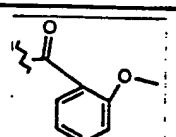
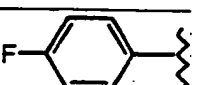
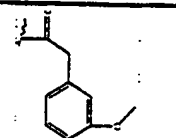
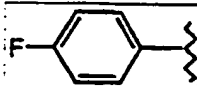
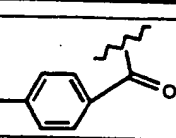
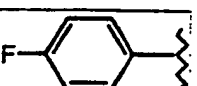
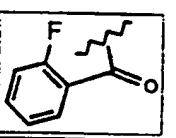
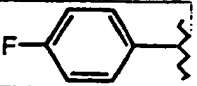
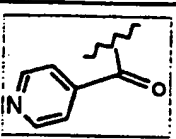
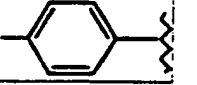
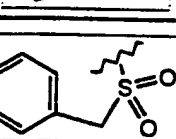
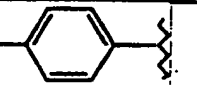
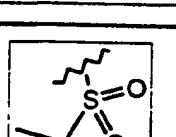


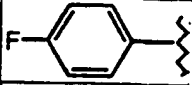
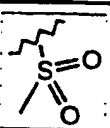
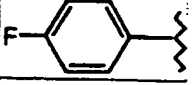
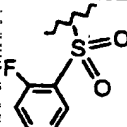
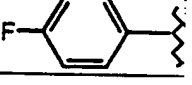
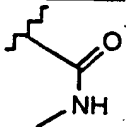
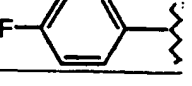
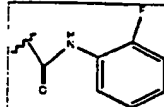
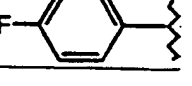
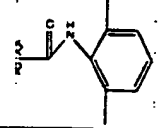
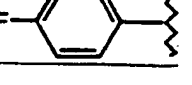
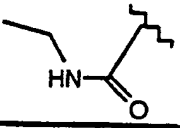
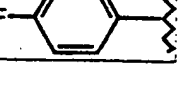
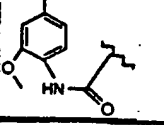
Examples B-1934 through B-1957 are prepared from Scaffold C-41

Example#      R<sup>2</sup>      R<sup>4</sup>

B-1934					
B-1935					
B-1936					
B-1937					
B-1938					
B-1939					
B-1940					

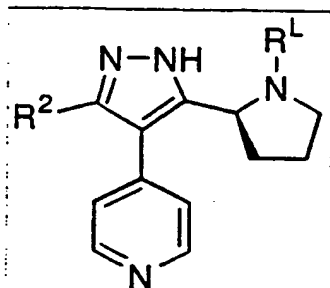
825

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1941					
B-1942					
B-1943					
B-1944					
B-1945					
B-1946					
B-1947					
B-1948					
B-1949					
B-1950					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1951					
B-1952					
B-1953					
B-1954					
B-1955					
B-1956					
B-1957					



827



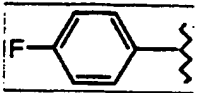
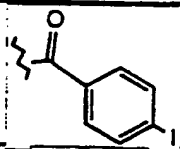
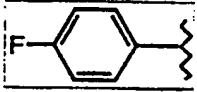
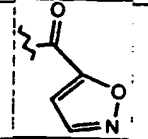
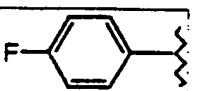
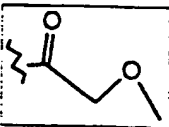
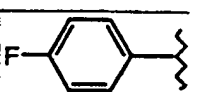
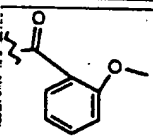
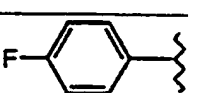
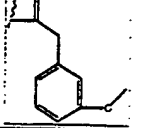
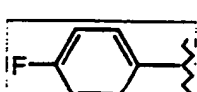
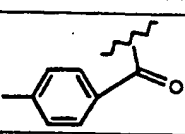
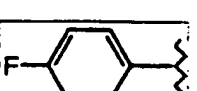
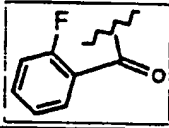
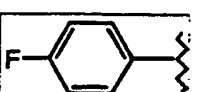
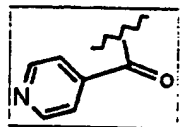
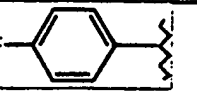
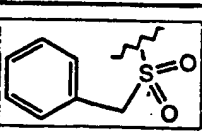
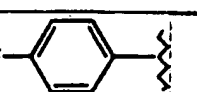
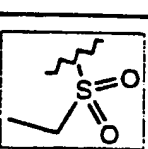
Examples B-1958 through B-1981 are prepared from Scaffold C-43

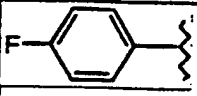
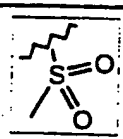
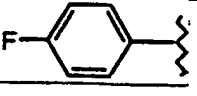
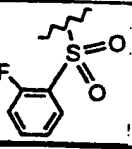
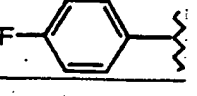
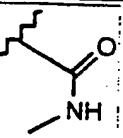
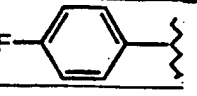
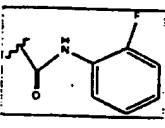
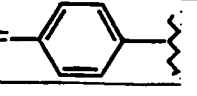
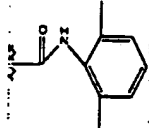
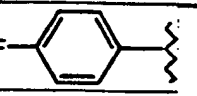
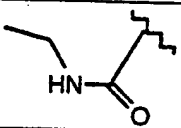
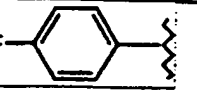
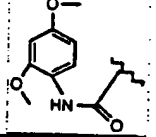
Example#	$R^2$	$R^1$			
B-1958					
B-1959					
B-1960					
B-1961					
B-1962					
B-1963					
B-1964					

828

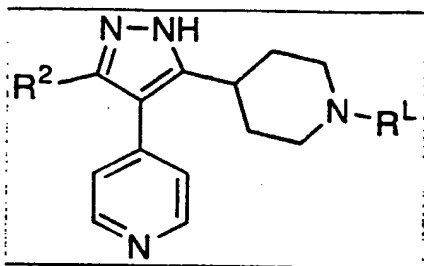
Example#

 $R^2$  $R^L$ 

B-1965					
B-1966					
B-1967					
B-1968					
B-1969					
B-1970					
B-1971					
B-1972					
B-1973					
B-1974					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1975					
B-1976					
B-1977					
B-1978					
B-1979					
B-1980					
B-1981					

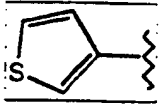
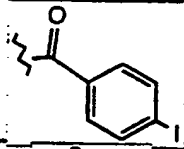
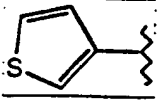
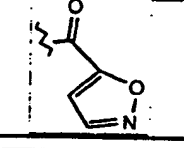
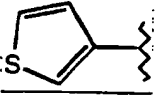
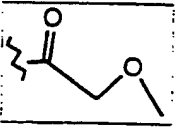
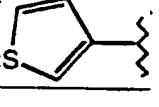
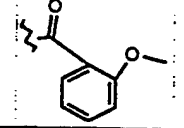
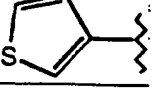
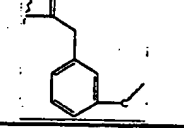
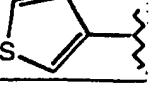
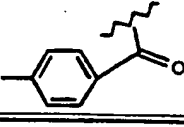
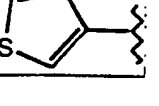
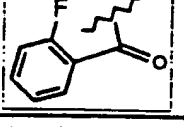
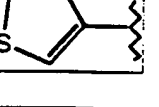
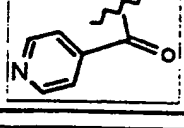
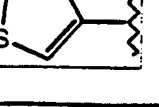
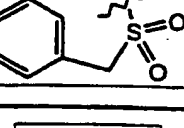
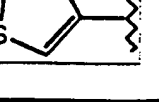
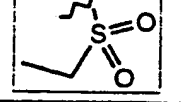
830

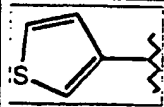
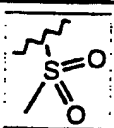
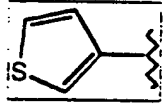
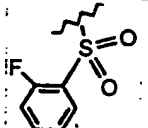
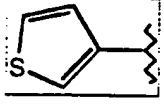
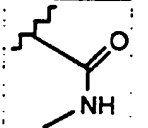
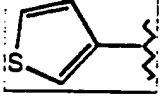
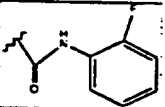
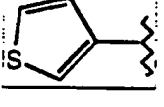
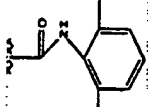
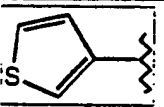
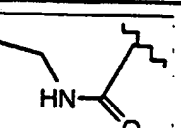
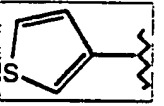
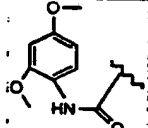


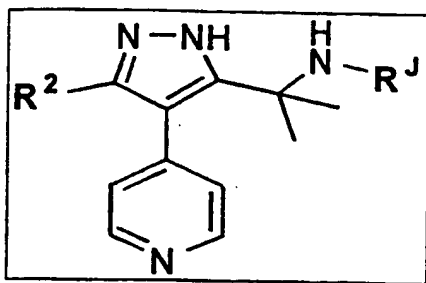
Examples B-1982 through B-2005 are prepared from Scaffold C-30

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1982					
B-1983					
B-1984					
B-1985					
B-1986					
B-1987					
B-1988					

831

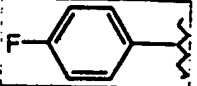
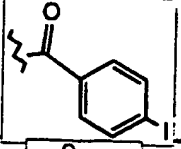
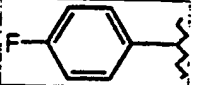
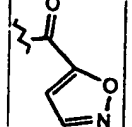
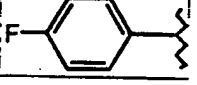
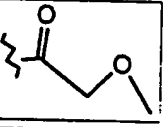
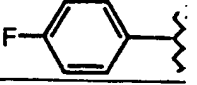
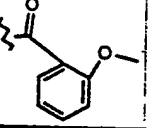
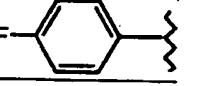
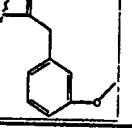
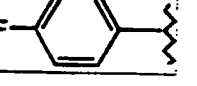
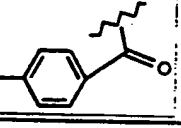
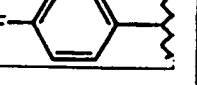
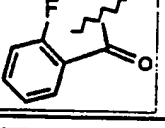
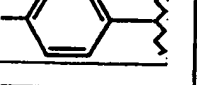
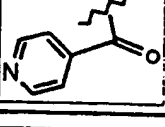
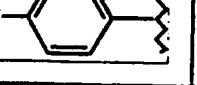
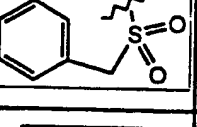
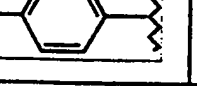
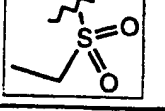
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1989					
B-1990					
B-1991					
B-1992					
B-1993					
B-1994					
B-1995					
B-1996					
B-1997					
B-1998					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1999					
B-2000					
B-2001					
B-2002					
B-2003					
B-2004					
B-2005					

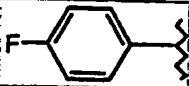
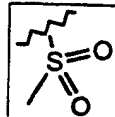
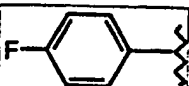
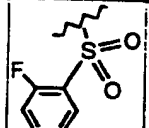
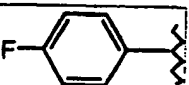
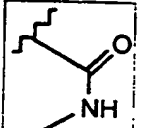
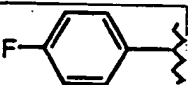
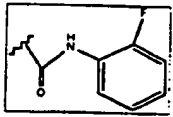
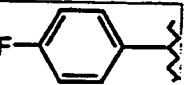
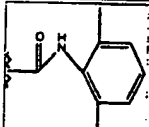
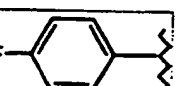
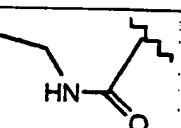
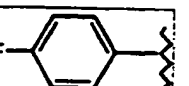
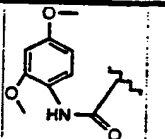


Examples B-2006 through B-2029 are prepared from Scaffold C-60

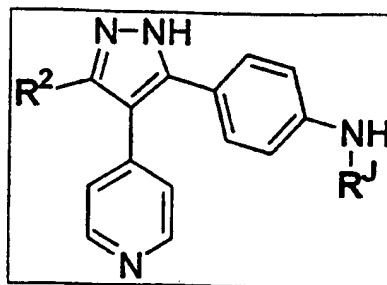
Example#	R <sup>2</sup>	R <sup>j</sup>			
B-2006					
B-2007					
B-2008					
B-2009					
B-2010					
B-2011					
B-2012					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2013					
B-2014					
B-2015					
B-2016					
B-2017					
B-2018					
B-2019					
B-2020					
B-2021					
B-2022					



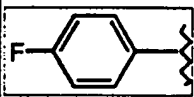
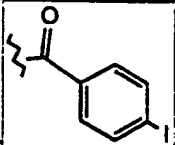
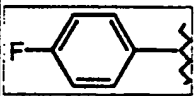
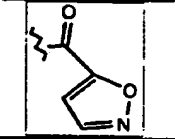
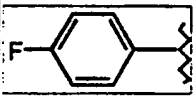
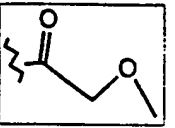
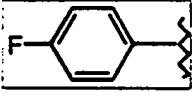
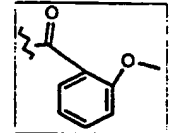
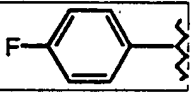
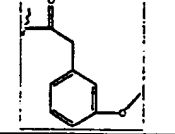
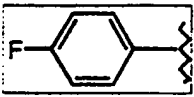
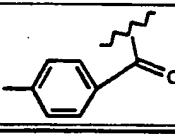
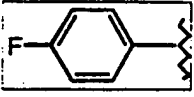
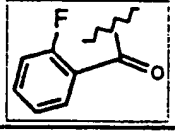
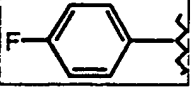
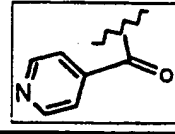
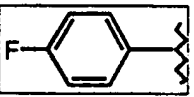
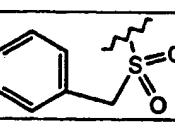
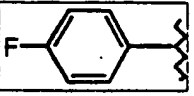
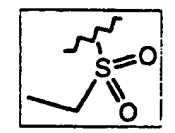
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2023					
B-2024					
B-2025					
B-2026					
B-2027					
B-2028					
B-2029					

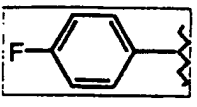
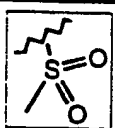
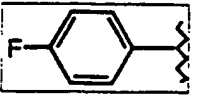
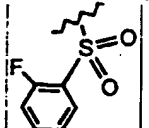
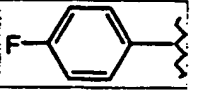
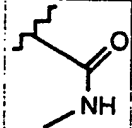
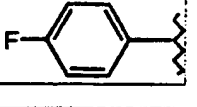
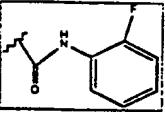
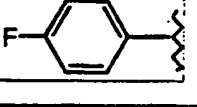
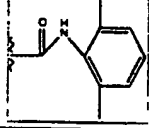
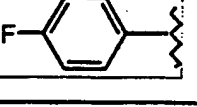
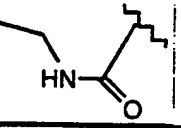
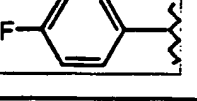
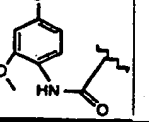
836

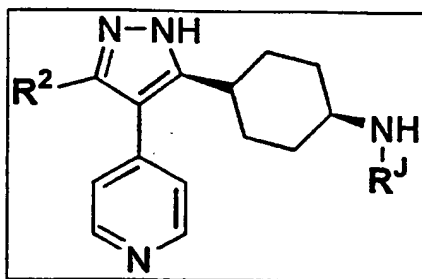


Examples B-2030 through B-2053 are prepared from Scaffold C-36

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2030					
B-2031					
B-2032					
B-2033					
B-2034					
B-2035					
B-2036					

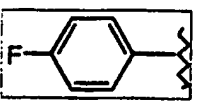
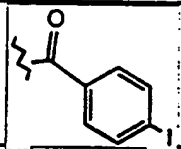
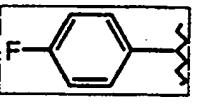
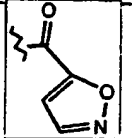
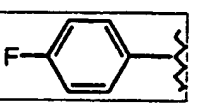
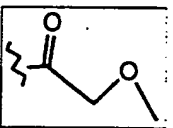
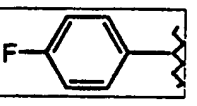
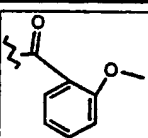
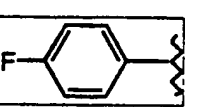
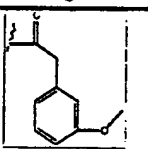
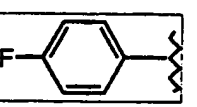
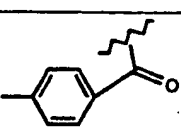
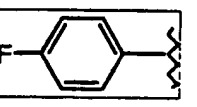
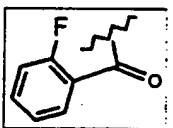
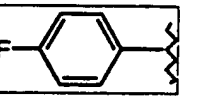
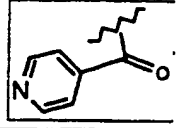
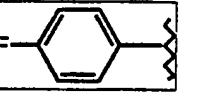
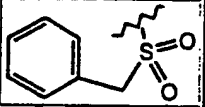
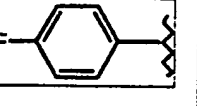
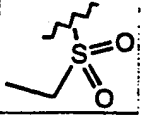
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2037					
B-2038					
B-2039					
B-2040					
B-2041					
B-2042					
B-2043					
B-2044					
B-2045					
B-2046					

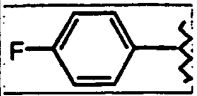
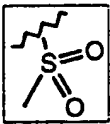
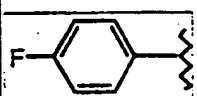
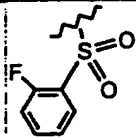
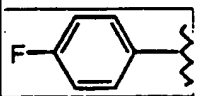
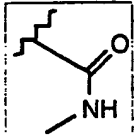
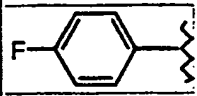
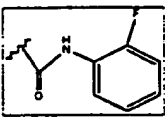
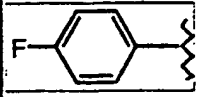
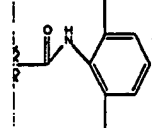
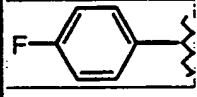
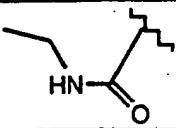
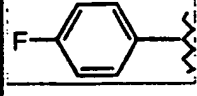
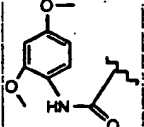
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2047					
B-2048					
B-2049					
B-2050					
B-2051					
B-2052					
B-2053					



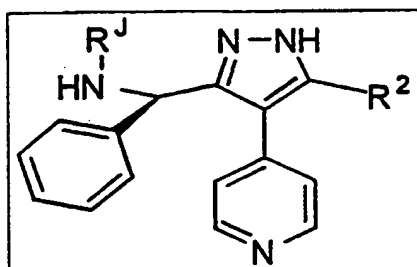
Examples B-2054 through B-2077 are prepared from Scaffold C-34

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2054					
B-2055					
B-2056					
B-2057					
B-2058					
B-2059					
B-2060					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2061					
B-2062					
B-2063					
B-2064					
B-2065					
B-2066					
B-2067					
B-2068					
B-2069					
B-2070					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2071					
B-2072					
B-2073					
B-2074					
B-2075					
B-2076					
B-2077					

842



Examples B-2078 through B-2101 are prepared from Scaffold C-57

Example#

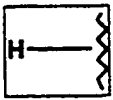
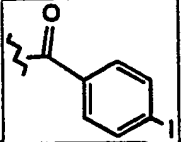
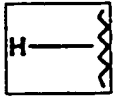
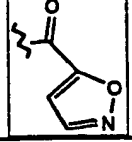
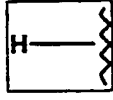
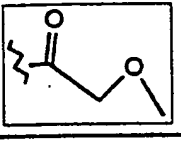
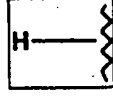
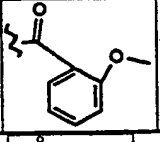
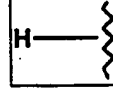
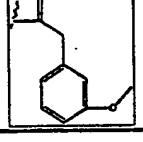
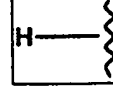
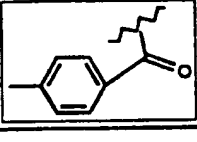
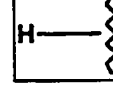
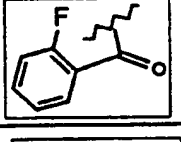
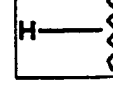
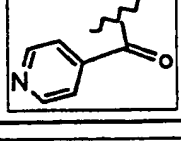
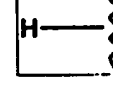
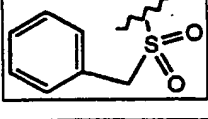
 $R^2$  $R^J$ 

B-2078					
B-2079					
B-2080					
B-2081					
B-2082					
B-2083					
B-2084					



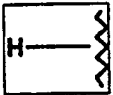
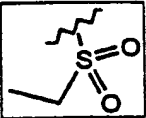
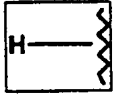
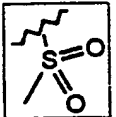
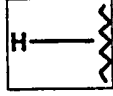
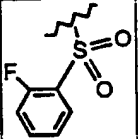
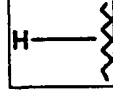
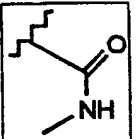
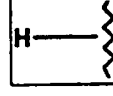
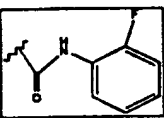
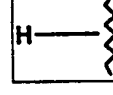
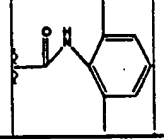

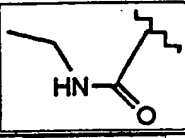
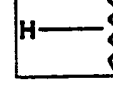
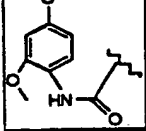
Example#

 $R^2$  $R^1$ 

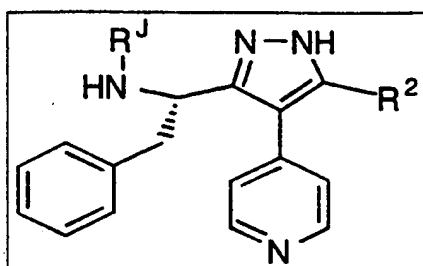
B-2085					
B-2086					
B-2087					
B-2088					
B-2089					
B-2090					
B-2091					
B-2092					
B-2093					

Example#

 $R^2$  $R^1$ 

B-2094					
B-2095					
B-2096					
B-2097					
B-2098					
B-2099					
B-2100					
B-2101					

845

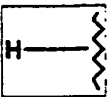
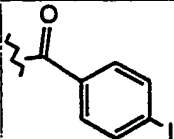
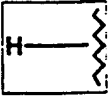
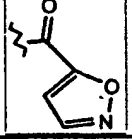
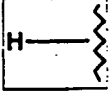
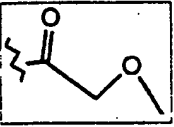
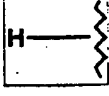
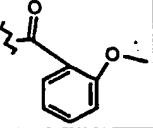
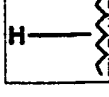
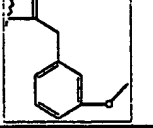
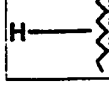
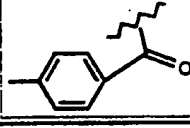
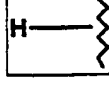
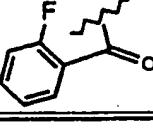
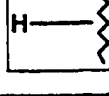
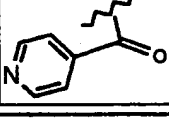
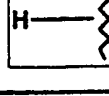
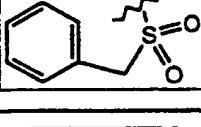
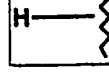
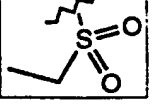


Examples B-2102 through B-2125 are prepared from Scaffold C-52

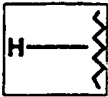
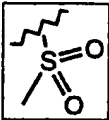
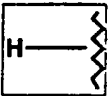
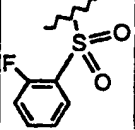
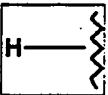
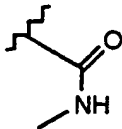
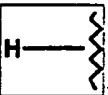
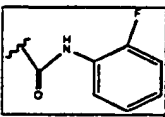
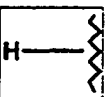
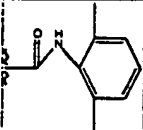
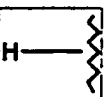
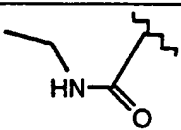
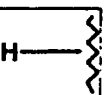
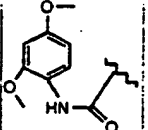
Example#	$R^2$	$R^J$			
B-2102					
B-2103					
B-2104					
B-2105					
B-2106					
B-2107					
B-2108					

Example#

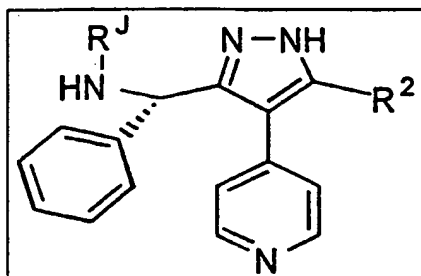
 $R^2$  $R^1$ 

B-2109					
B-2110					
B-2111					
B-2112					
B-2113					
B-2114					
B-2115					
B-2116					
B-2117					
B-2118					

847

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2119					
B-2120					
B-2121					
B-2122					
B-2123					
B-2124					
B-2125					

848

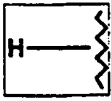
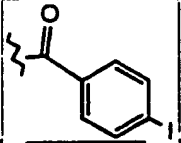
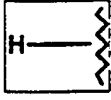
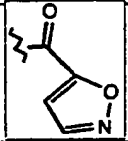
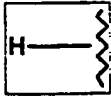
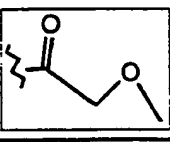
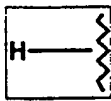
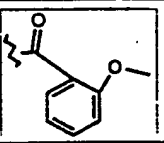
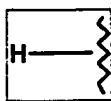
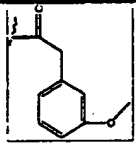
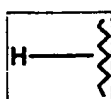
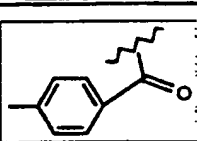
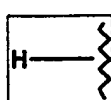
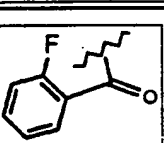
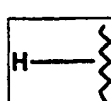
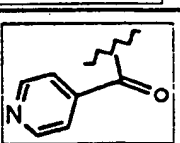
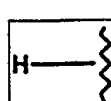
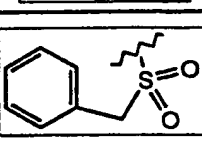
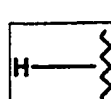
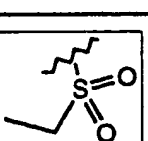


Examples B-2126 through B-2149 are prepared from Scaffold C-56

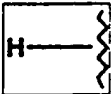
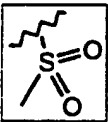
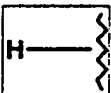
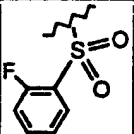
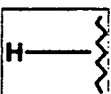
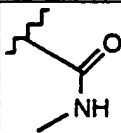
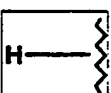
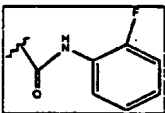
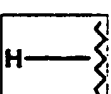
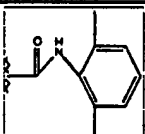
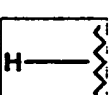
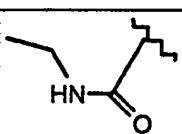
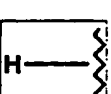
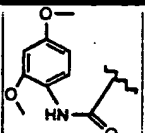
Example#

 $R^2$  $R^J$ 

B-2126					
B-2127					
B-2128					
B-2129					
B-2130					
B-2131					
B-2132					

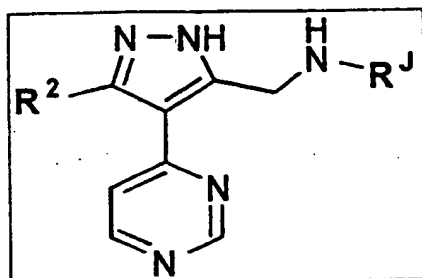
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2133					
B-2134					
B-2135					
B-2136					
B-2137					
B-2138					
B-2139					
B-2140					
B-2141					
B-2142					

850

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2143					
B-2144					
B-2145					
B-2146					
B-2147					
B-2148					
B-2149					

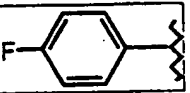
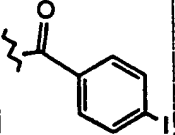
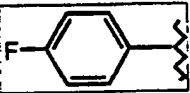
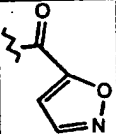
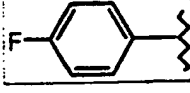
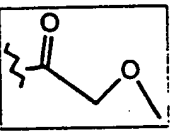
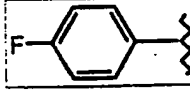
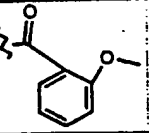
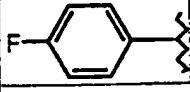
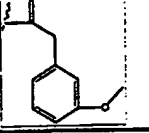
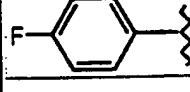
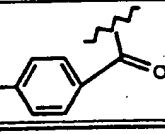
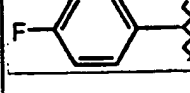
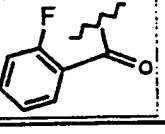
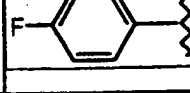
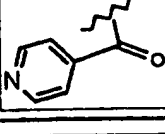
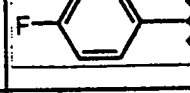
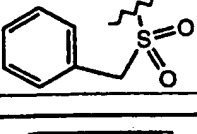
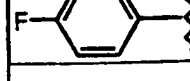
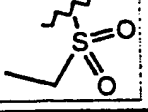


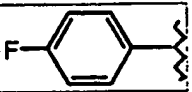
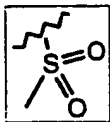
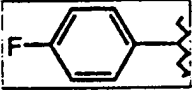
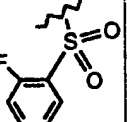
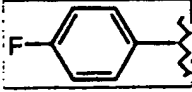
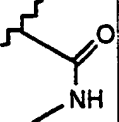
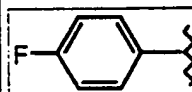
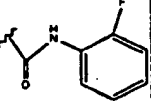
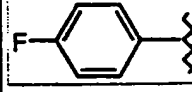
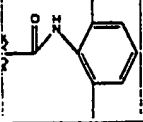
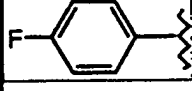
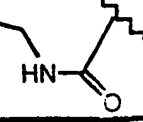
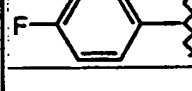
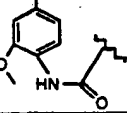
851



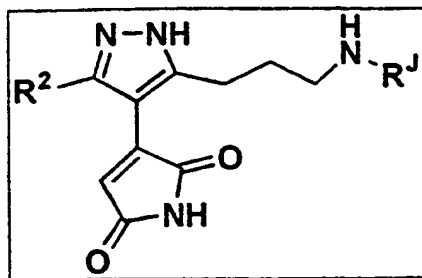
Examples B-2150 through B-2173 are prepared from Scaffold C-32

Example#	$R^2$	$R^J$			
B-2150					
B-2151					
B-2152					
B-2153					
B-2154					
B-2155					
B-2156					

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2157					
B-2158					
B-2159					
B-2160					
B-2161					
B-2162					
B-2163					
B-2164					
B-2165					
B-2166					

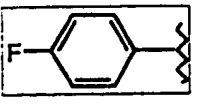
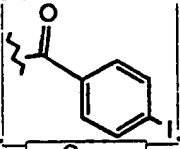
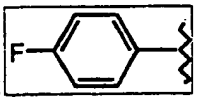
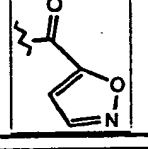
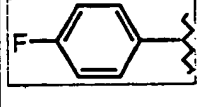
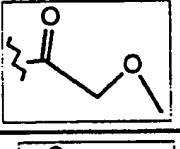
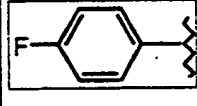
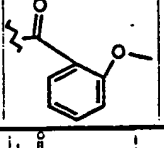
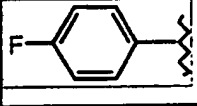
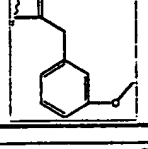
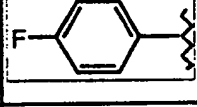
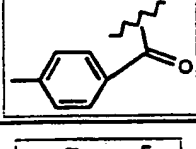
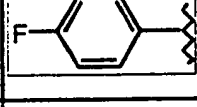
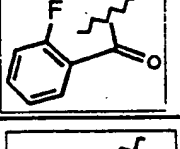
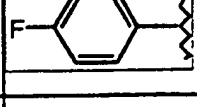
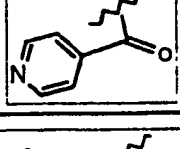
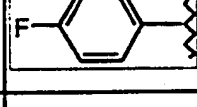
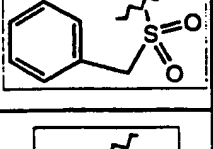
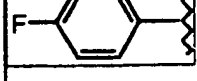
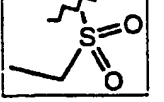
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2167					
B-2168					
B-2169					
B-2170					
B-2171					
B-2172					
B-2173					

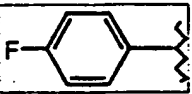
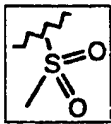
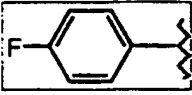
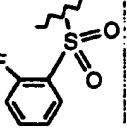
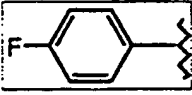
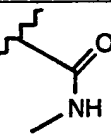
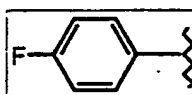
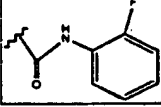
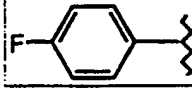
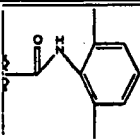
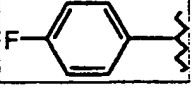
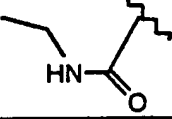
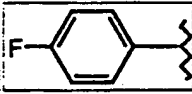
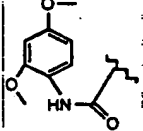
854



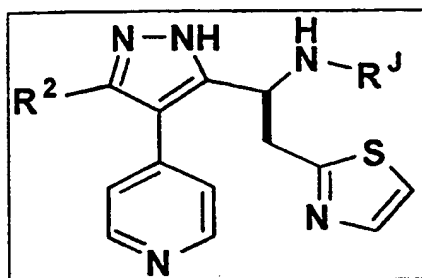
Examples 2174 through B-2197 are prepared from Scaffold C-64

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2174					
B-2175					
B-2176					
B-2177					
B-2178					
B-2179					
B-2180					

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2181					
B-2182					
B-2183					
B-2184					
B-2185					
B-2186					
B-2187					
B-2188					
B-2189					
B-2190					

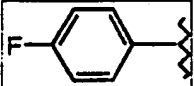
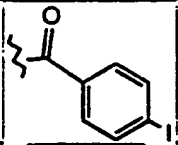
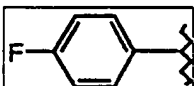
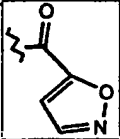
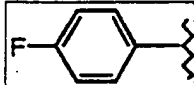
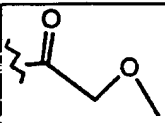
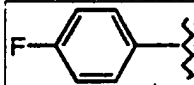
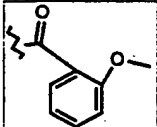
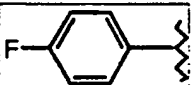
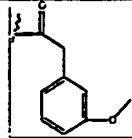
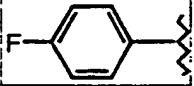
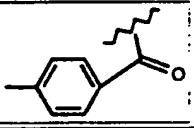
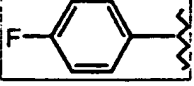
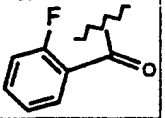
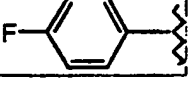
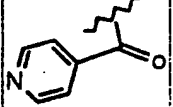
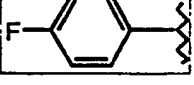
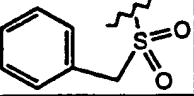
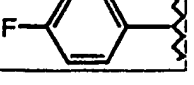
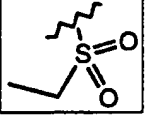
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2191					
B-2192					
B-2193					
B-2194					
B-2195					
B-2196					
B-2197					

857

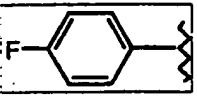
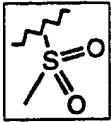
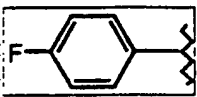
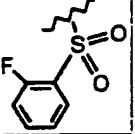
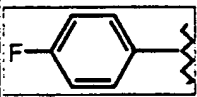
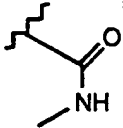
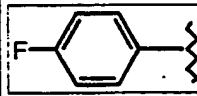
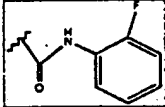
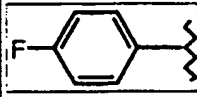
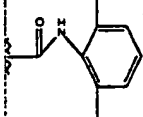
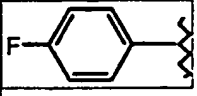
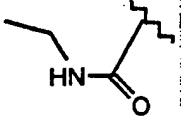
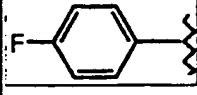
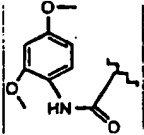


Examples B-2198 through B-2221 re prepared from Scaffold C-22

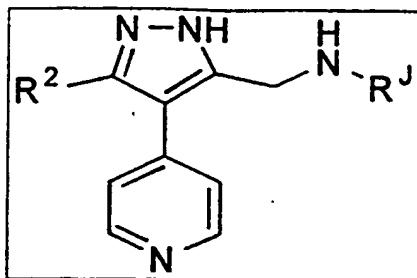
Example#	$R^2$	$R^J$			
B-2198					
B-2199					
B-2200					
B-2201					
B-2202					
B-2203					
B-2204					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2205					
B-2206					
B-2207					
B-2208					
B-2209					
B-2210					
B-2211					
B-2212					
B-2213					
B-2214					



Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2215					
B-2216					
B-2217					
B-2218					
B-2219					
B-2220					
B-2221					

860

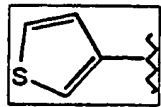
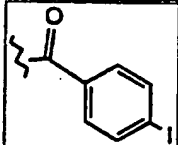
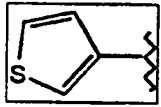
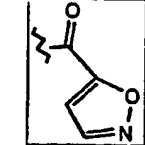
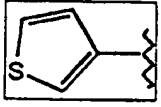
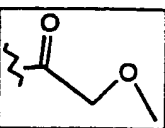
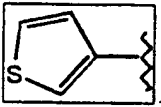
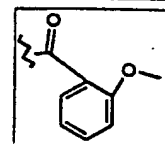
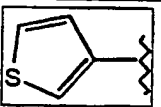
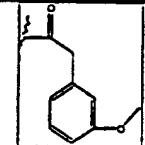
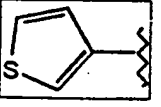
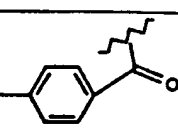
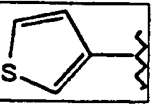
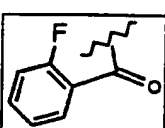
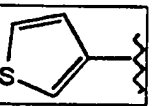
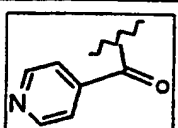
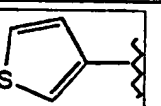
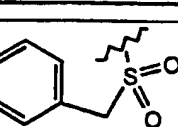


Examples B-2222 through B-2245 are prepared from Scaffold C-29

Example#

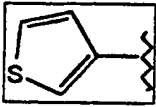
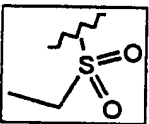
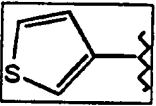
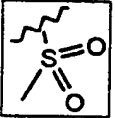
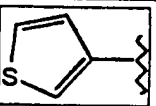
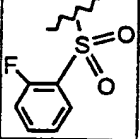
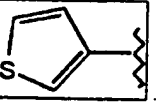
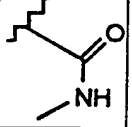
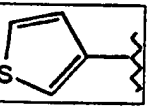
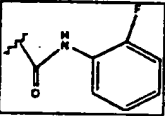
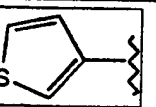
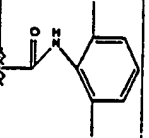
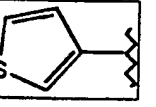
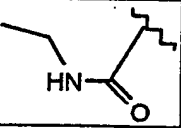
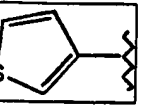
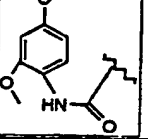
 $R^2$  $R^J$ 

B-2222					
B-2223					
B-2224					
B-2225					
B-2226					
B-2227					
B-2228					

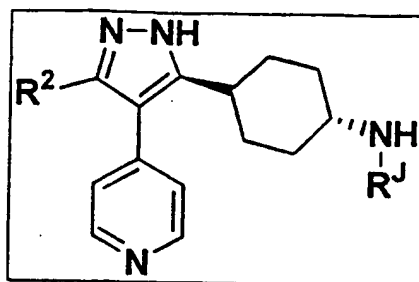
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2229					
B-2230					
B-2231					
B-2232					
B-2233					
B-2234					
B-2235					
B-2236					
B-2237					

Example#

 $R^2$  $R^1$ 

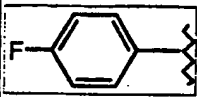
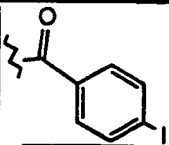
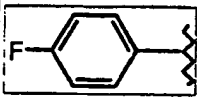
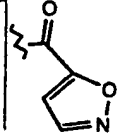
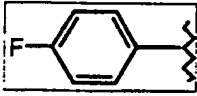
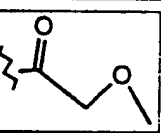
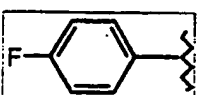
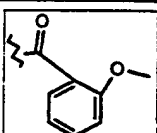
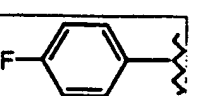
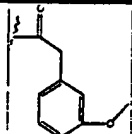
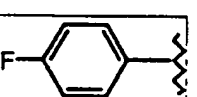
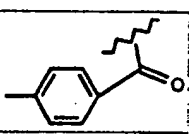
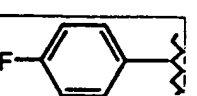
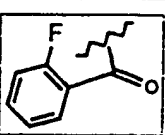
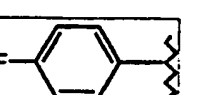
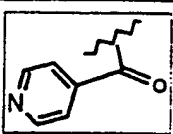
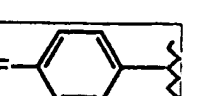
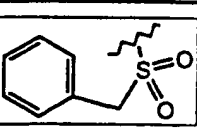
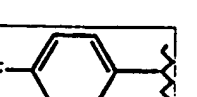
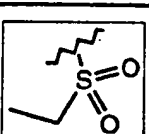
B-2238					
B-2239					
B-2240					
B-2241					
B-2242					
B-2243					
B-2244					
B-2245					

863

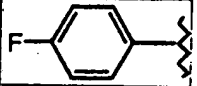
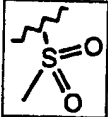
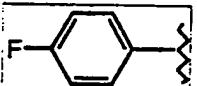
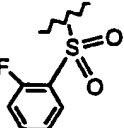
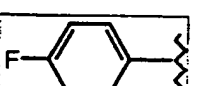
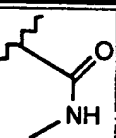
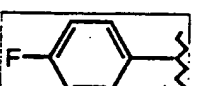
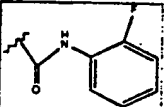
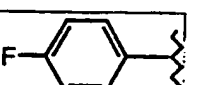
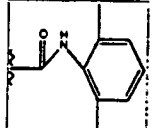
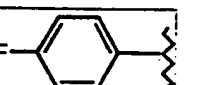
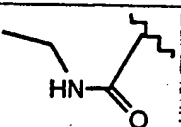
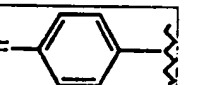
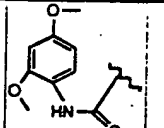


Examples B-2246 through B-2269 are prepared from Scaffold C-35

Example#	R²	R'			
B-2246					
B-2247					
B-2248					
B-2249					
B-2250					
B-2251					
B-2252					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2253					
B-2254					
B-2255					
B-2256					
B-2257					
B-2258					
B-2259					
B-2260					
B-2261					
B-2262					

865

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2263					
B-2264					
B-2265					
B-2266					
B-2267					
B-2268					
B-2269					

5

10

**Examples B-2270 through B-2317**

15

In a parallel array reaction block containing 48 fritted vessels, each reaction vessel was charged with 250 mg of polymer bound carbodiimide B48 (1.0 mmol/g resin) and a solution of the acid-containing scaffold C-  
20 49 in dimethylformamide (0.1 M, 500 uL). To each slurry was added a solution of pyridine in dichloromethane (0.2 M, 1000 uL) followed by a solution of a unique amine B47 (0.2 M, 375 uL) in dimethylformamide. The reaction mixtures were agitated on a Labline benchtop orbital  
25 shaker at 250 RPM for 16-20 h at ambient temperature. The reaction mixtures were filtered into conical vials and the polymer was washed with 1.5 mL of dimethylformamide and 2.0 mL of dichloromethane. The filtrates were evaporated to dryness in a Savant  
30 apparatus and dimethylformamide (350 uL) was added to each conical vial to dissolve the residue. A solution of tetrafluorophthalic anhydride (1.0 M, 150 uL) in



867

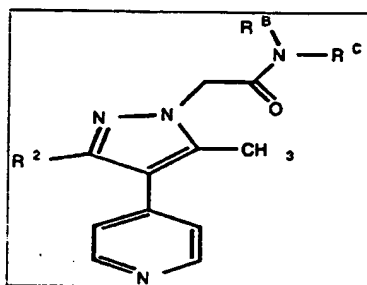
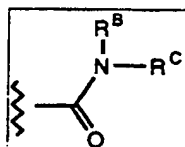
dimethylformamide was added to the reconstituted conical vials and the mixture incubated for 2 hours at ambient temperature. Polyamine polymer B33 (4.0 meq N/g resin, 250 mg) and 1.0 mL dichloromethane was then added to the  
5 reaction mixture in each conical vial. After agitating the reaction mixtures for 16 h at 250 RPM on an orbital shaker at ambient temperature, the mixtures were filtered through a polypropylene syringe tube fitted with a porous frit. The polymers were washed twice with  
10 dimethylformamide (1.0 mL each) and the filtrates and washings collected in conical vials. The filtrates were evaporated to dryness and weighed to afford the desired amide products B-2270 through B-2317 as oils or solids. The analytical data and yields for the products prepared  
15 in this manner are listed below.

20

25

30

868

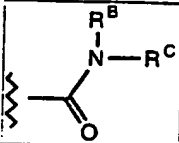
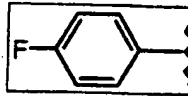
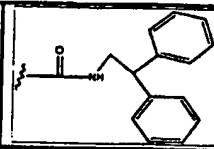
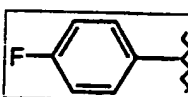
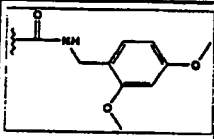
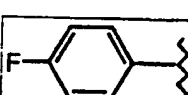
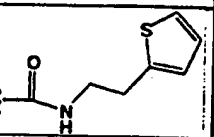
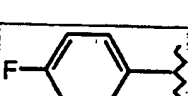
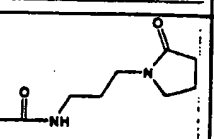
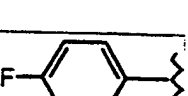
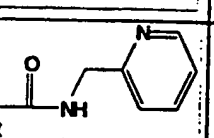
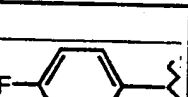
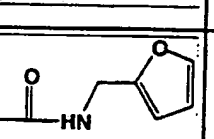

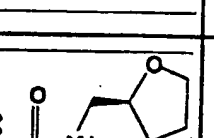

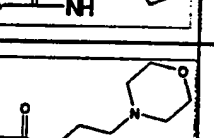

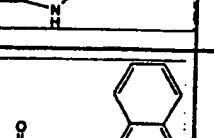

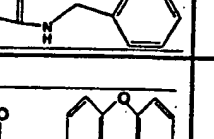
R<sup>2</sup>

Yield

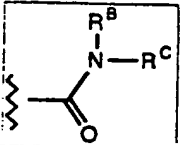
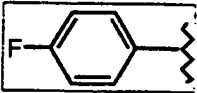
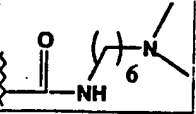
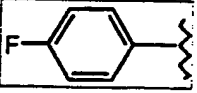

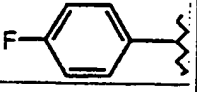
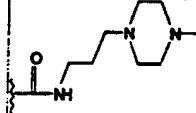
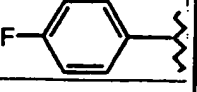
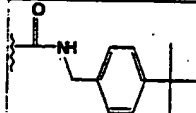
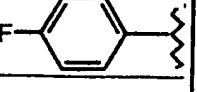
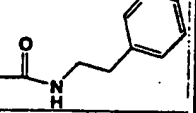
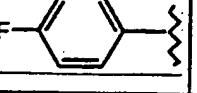
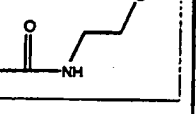
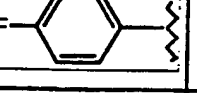
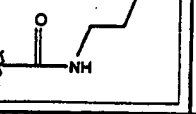
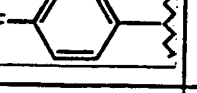
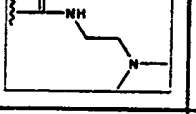
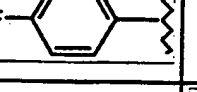
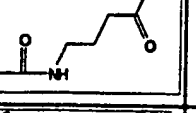
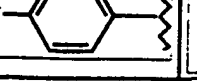
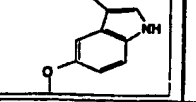
Calcd. Mass  
Spec.Observed  
Mass Spec  
M+H

B-2270			12	352	353
B-2271			39	432	433
B-2272			26	400	-
B-2273			14	396	397
B-2274			30	434	435
B-2275			43	443	-
B-2276			35	364	365

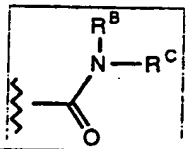
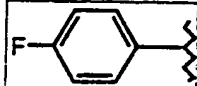
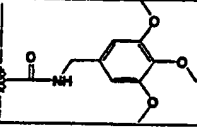
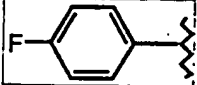
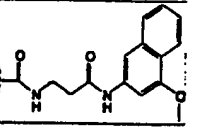
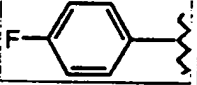
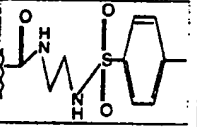
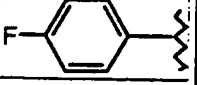
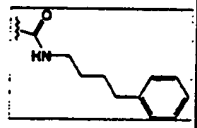
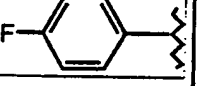
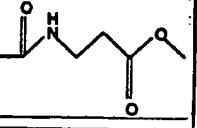
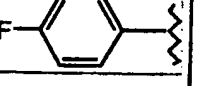
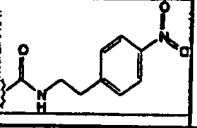
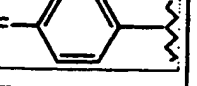
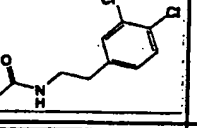
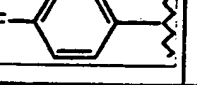
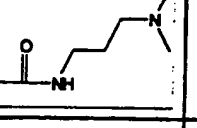
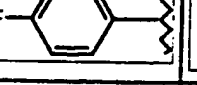
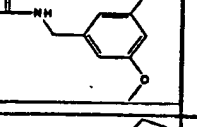
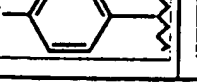

869

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2277			33	490	-
B-2278			53	460	461
B-2279			10	420	-
B-2280			7	435	436
B-2281			18	401	402
B-2282			22	390	413 <sup>a</sup> <sup>a</sup> M+Na
B-2283			10	394	417 <sup>a</sup> <sup>a</sup> M+Na
B-2284			7	423	-
B-2285			23	450	-
B-2286			4	506	-

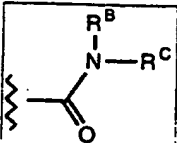
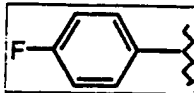
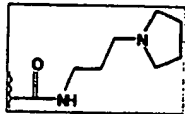
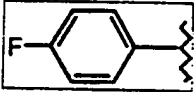
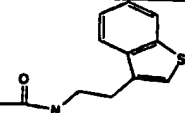
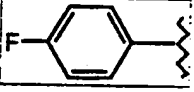
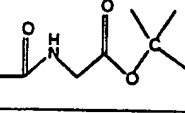
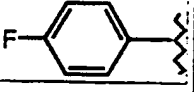
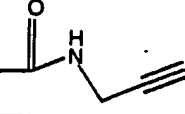
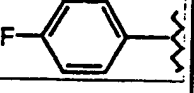
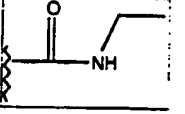
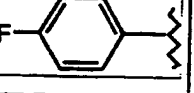
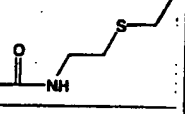
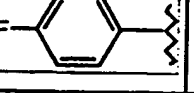
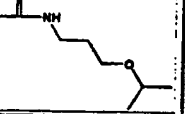
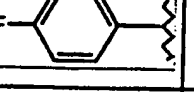
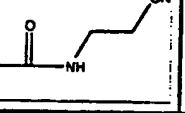
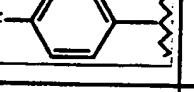
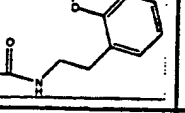
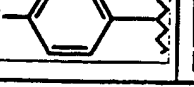
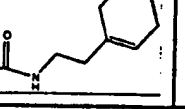
870

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2287			5	437	438
B-2288			8	435	436
B-2289			4	450	451
B-2290			9	456	457
B-2291			9	415	416
B-2292			5	368	369
B-2293			5	366	367
B-2294			5	381	382
B-2295			16	410	411
B-2296			4	483	-

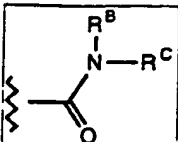
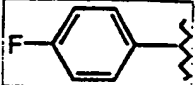
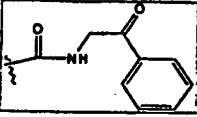
871

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2297			7	490	-
B-2298			4	537	-
B-2299			4	507	508
B-2300			7	442	-
B-2301			20	396	397
B-2302			30	459	-
B-2303			6	482	-
B-2304			5	395	396
B-2305			10	460	-
B-2306			11	466	467

872

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2307			5	421	422
B-2308			26	470	-
B-2309			24	424	425
B-2310			9	348	-
B-2311			21	338	339
B-2312			28	398	399
B-2313			6	410	-
B-2314			15	363	364
B-2315			11	444	-
B-2316			11	418	-

873

$R^2$			Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2317			36	428	-

874

5

10

By analogy to the procedure identified above for the preparation of Examples B-2270 through B-2317, the following examples B-2318 through B-2461 were prepared.

15

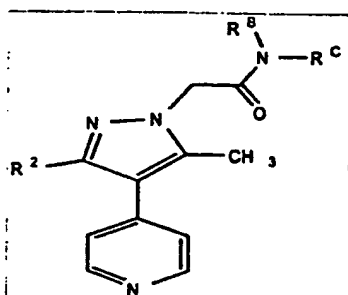
20

25

30

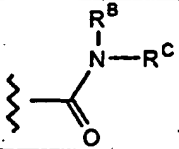
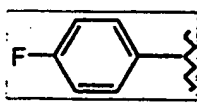
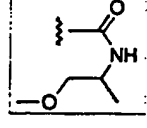
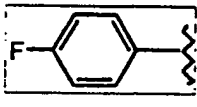
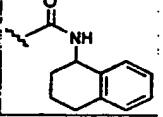
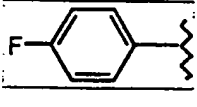
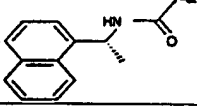
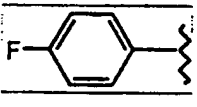
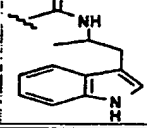
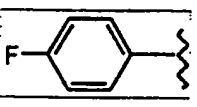
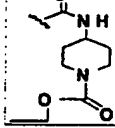
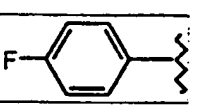
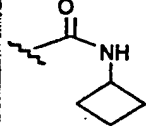
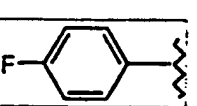
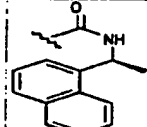
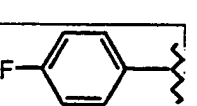
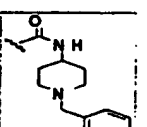
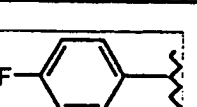
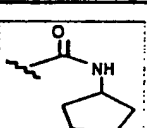


875

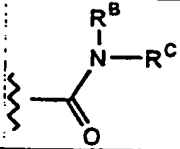
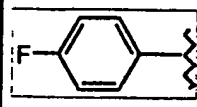
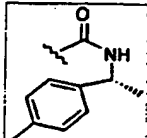
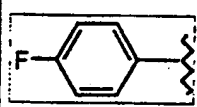
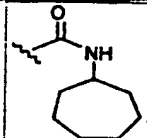
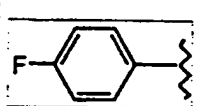
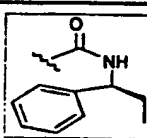
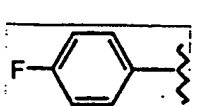
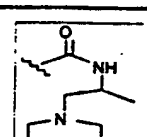
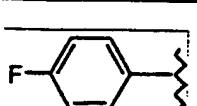
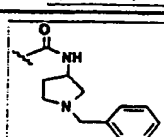
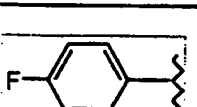
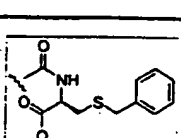
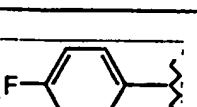
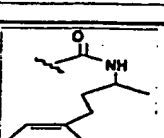
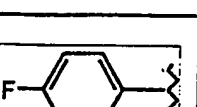
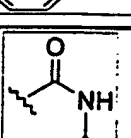
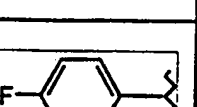
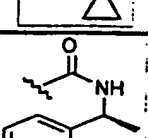


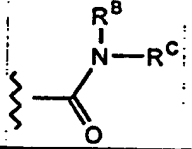
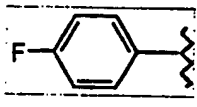
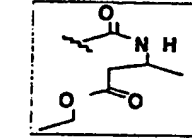
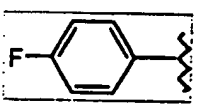
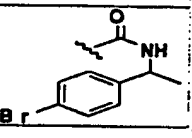
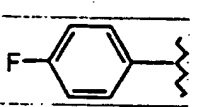
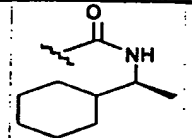
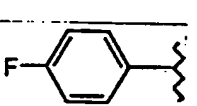
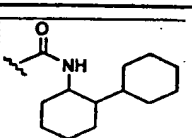
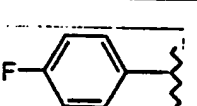
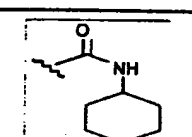
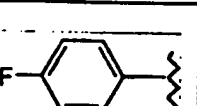
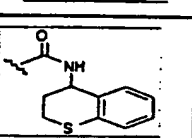
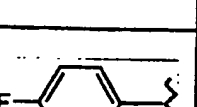
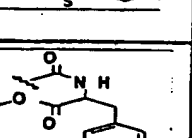
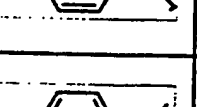
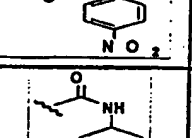

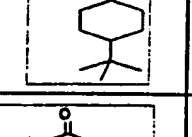
	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2318			23	426	427
B-2319			23	394	-
B-2320			50	490	491
B-2321			49	426	427
B-2322			40	366	367
B-2323			68	410	411
B-2324			57	456	457

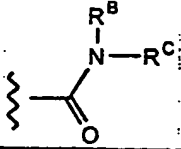
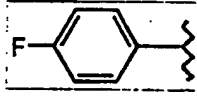
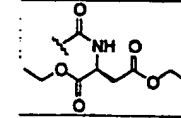
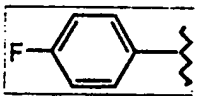
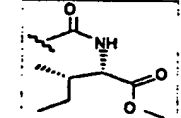
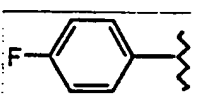
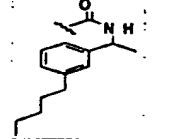
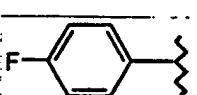
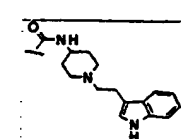
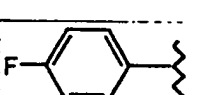
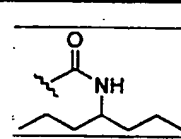
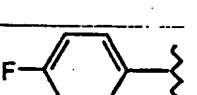
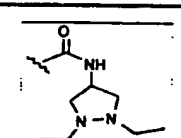
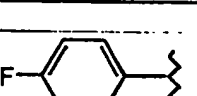
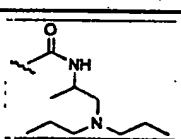
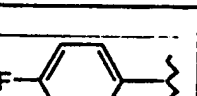
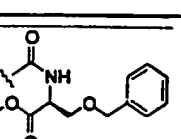
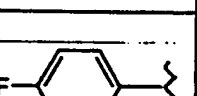
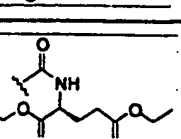
876

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2325			41	382	383
B-2326			71	440	441
B-2327			36	464	465
B-2328			32	467	468
B-2329			34	465	466
B-2330			26	364	365
B-2331			38	464	465
B-2332			33	483	484
B-2333			36	378	379

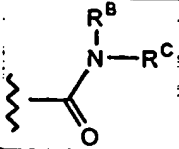
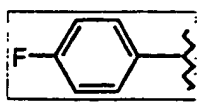
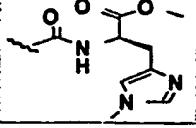
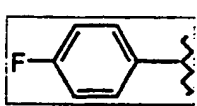
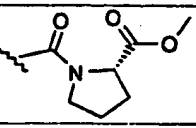
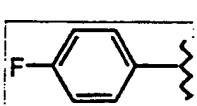
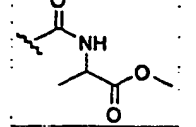
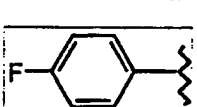
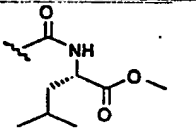
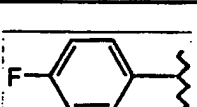
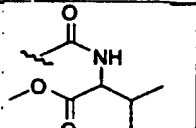
877

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2334			44	428	429
B-2335			27	406	407
B-2336			41	428	429
B-2337			27	423	424
B-2338			33	469	470
B-2339			52	518	519
B-2340			64	442	443
B-2341			41	350	351
B-2342			34	414	415

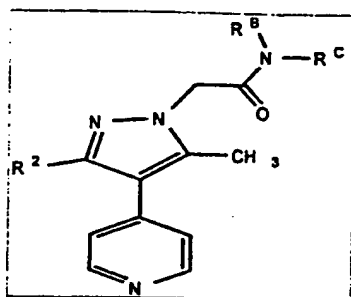
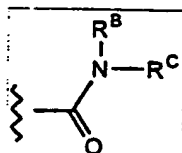
	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2343			29	424	425
B-2344			33	492	493
B-2345			30	420	421
B-2346			35	474	475
B-2347			34	392	393
B-2348			51	458	459
B-2349			73	517	518
B-2350			22	448	449
B-2351			64	486	487

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2352			41	482	483
B-2353			57	438	439
B-2354			63	484	485
B-2355			28	536	537
B-2356			29	408	409
B-2357			41	436	437
B-2358			41	451	452
B-2359			57	502	503
B-2360			46	496	497

880

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2361			13	476	477
B-2362			46	493	494
B-2363			57	396	397
B-2364			61	438	439
B-2365			72	424	425

881

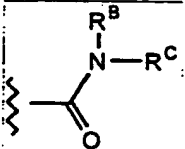
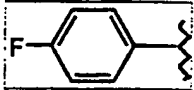
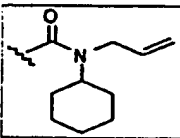
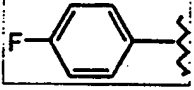
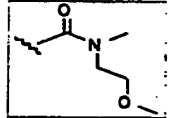
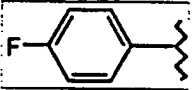
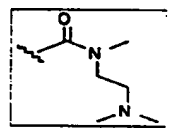
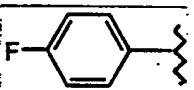
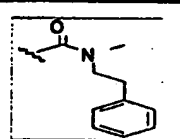
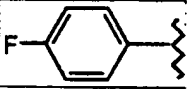
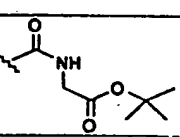
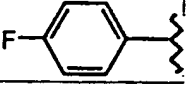
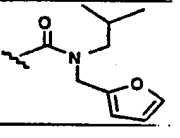
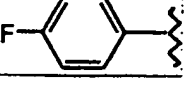
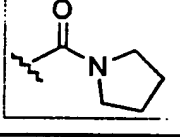
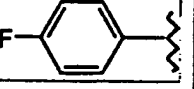
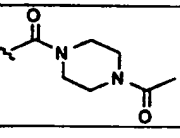
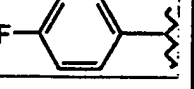
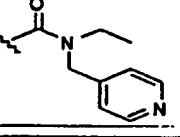
R<sup>2</sup>

Yield

Calcd. Mass  
Spec.Observed  
Mass Spec  
M+H

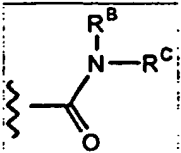
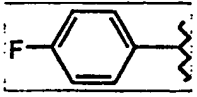
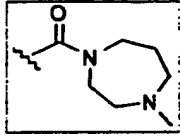
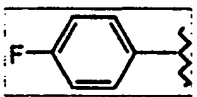
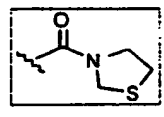
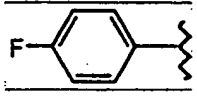
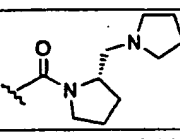
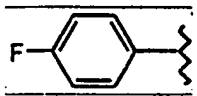
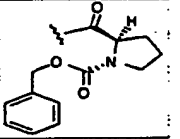
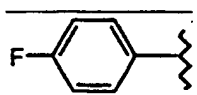
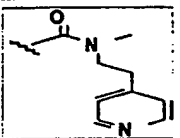
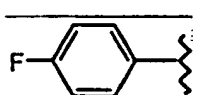
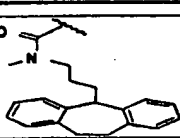
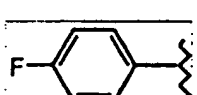
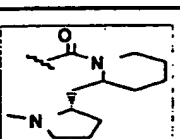
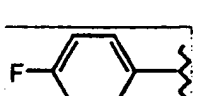
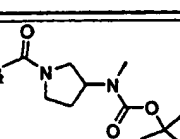
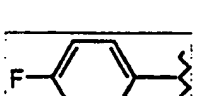
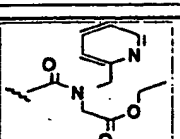
B-2366			34	380	381
B-2367			52	480	481
B-2368			35	407	407
B-2369			31	435	436
B-2370			33	414	415
B-2371			28	366	367
B-2372			37	422	423

882

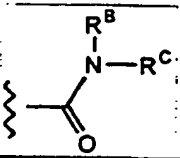
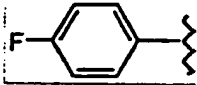
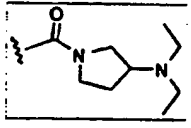
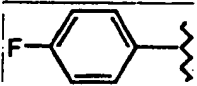
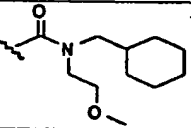
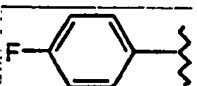
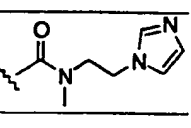
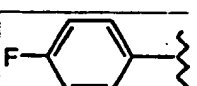
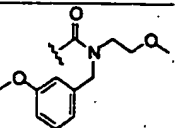
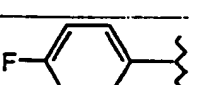
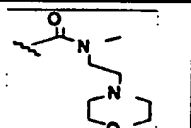
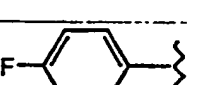
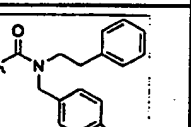
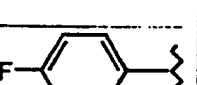
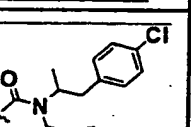
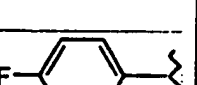
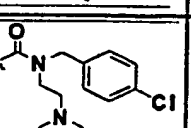
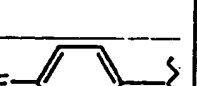
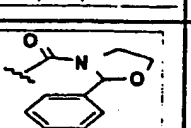
	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2373			50	432	433
B-2374			29	382	383
B-2375			35	395	396
B-2376			36	428	429
B-2377			68	438	439
B-2378			55	446	447
B-2379			33	364	365
B-2380			51	421	422
B-2381			52	429	430



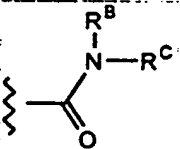
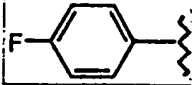
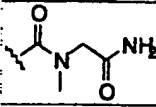
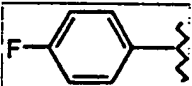
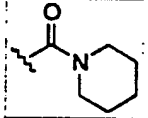
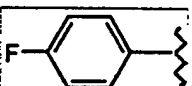
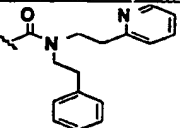
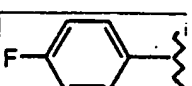
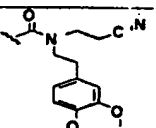
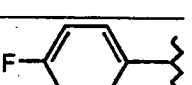
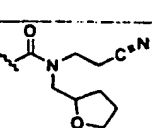
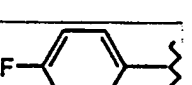
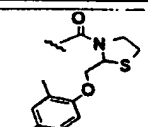
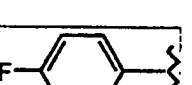
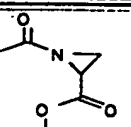
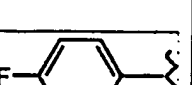
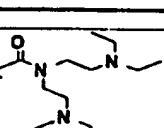

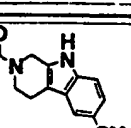
883

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2382			48	407	408
B-2383			53	382	383
B-2384			38	447	448
B-2385			59	498	450
B-2386			45	429	430
B-2387			74	558	-
B-2388			53	475	-
B-2389			33	493	494
B-2390			53	487	488

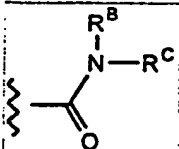
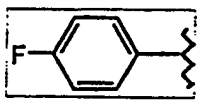
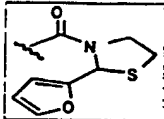
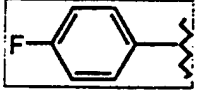
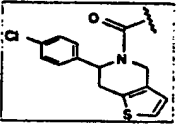
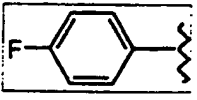
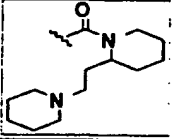
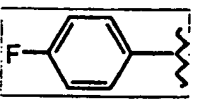
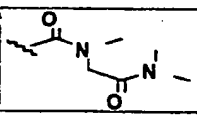
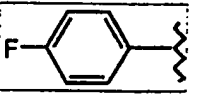
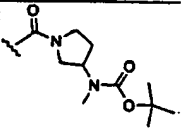
884

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2391			30	435	436
B-2392			57	464	465
B-2393			50	418	419
B-2394			65	488	489
B-2395			59	437	438
B-2396			34	534	535
B-2397			32	516	517
B-2398			81	533	534
B-2399			55	502	-

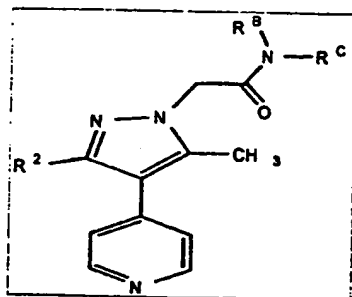
885

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2400			34	381	382
B-2401			32	378	379
B-2402			71	519	520
B-2403			68	527	528
B-2404			62	447	448
B-2405			71	536	537
B-2406			47	394	395
B-2407			65	508	509
B-2408			34	495	496

886

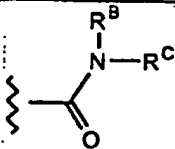
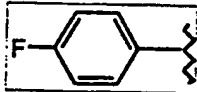
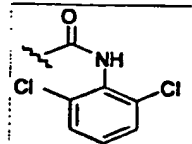
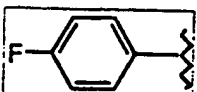
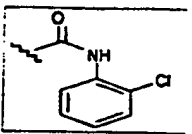
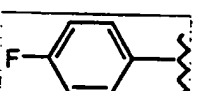
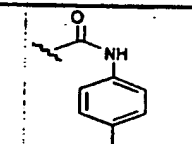
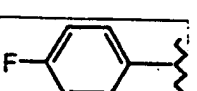
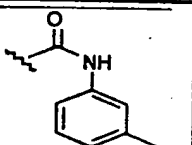
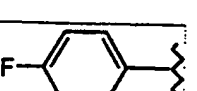
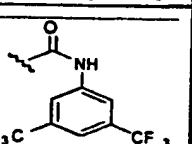
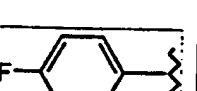
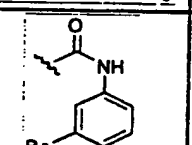
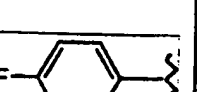
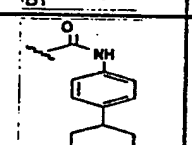
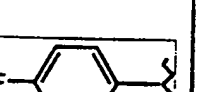
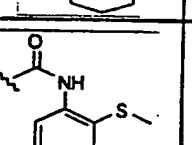

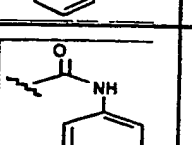
	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2409			47	448	449
B-2410			73	542	543
B-2411			81	489	490
B-2412			54	409	410
B-2413			37	493	494

887

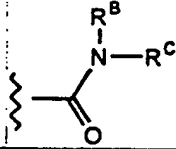
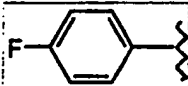
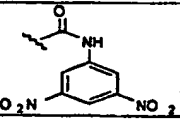
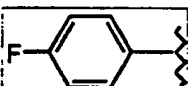
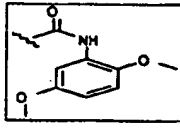
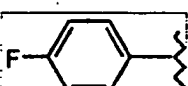
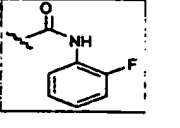
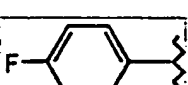
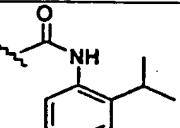
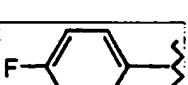
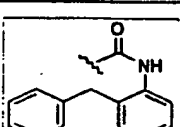
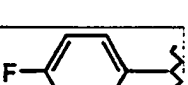
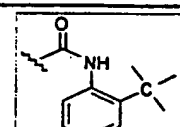
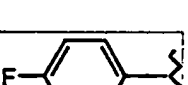
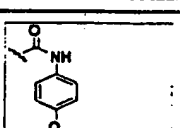
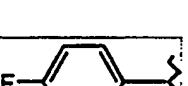
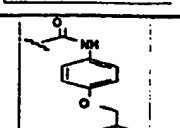

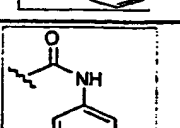


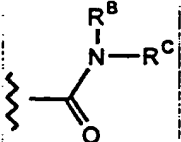
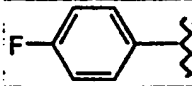
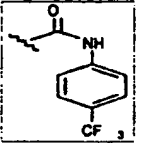
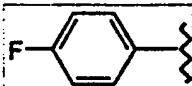
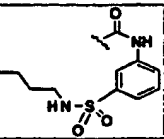

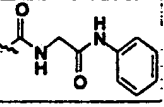
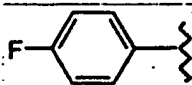
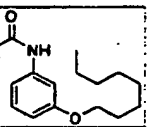
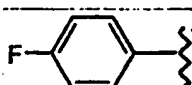
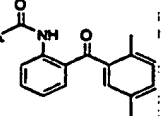
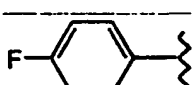
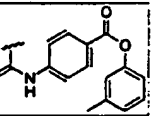
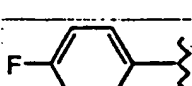
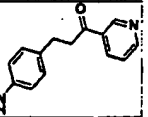
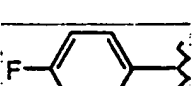
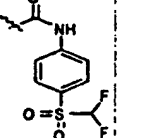
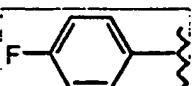
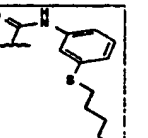
	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2414			14	473	474
B-2415			19	421	422
B-2416			13	386	387
B-2417			29	414	415
B-2418			6	420	421
B-2419			10	454	-
B-2420			5	442	443

888

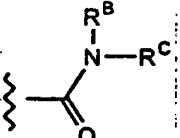
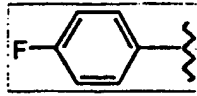
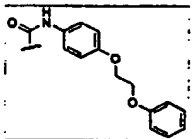
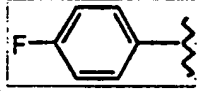
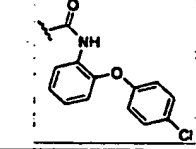
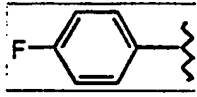
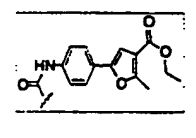
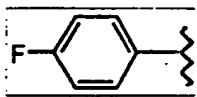
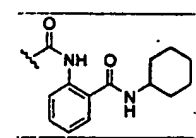
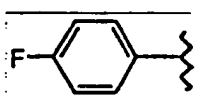
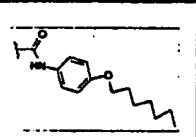
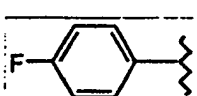
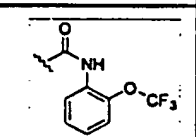
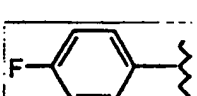
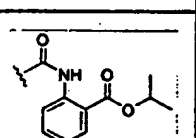
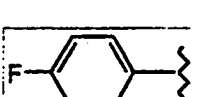
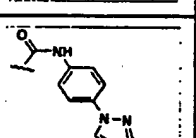
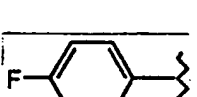
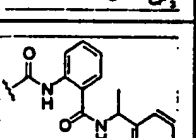
	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2421			28	454	455
B-2422			47	420	421
B-2423			53	400	401
B-2424			15	400	401
B-2425			18	522	523
B-2426			38	464	465
B-2427			26	468	469
B-2428			22	432	433
B-2429			41	404	405

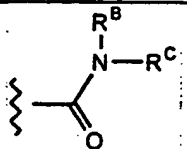
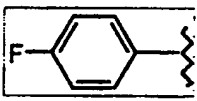
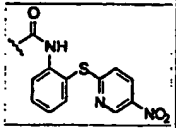
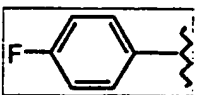
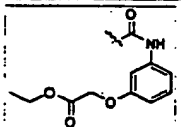
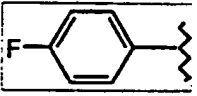
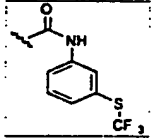
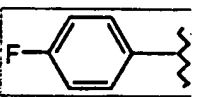
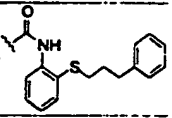
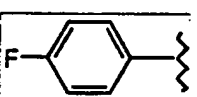
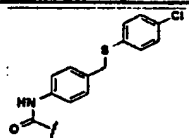
889

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2430			15	476	477
B-2431			6	446	447
B-2432			37	404	405
B-2433			8	428	429
B-2434			13	476	477
B-2435			23	442	443
B-2436			5	486	487
B-2437			4	492	493
B-2438			58	422	423

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2439			12	454	455
B-2440			8	521	522
B-2441			6	443	444
B-2442			37	514	515
B-2443			15	518	-
B-2444			52	520	-
B-2445			33	517	518
B-2446			70	500	501
B-2447			56	488	489



	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2448			51	522	523
B-2449			19	512	513
B-2450			16	538	539
B-2451			71	511	512
B-2452			71	500	501
B-2453			61	470	-
B-2454			15	472	473
B-2455			39	520	-
B-2456			51	533	534

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2457			55	540	-
B-2458			22	488	489
B-2459			8	486	487
B-2460			13	534	535
B-2461			13	542	-

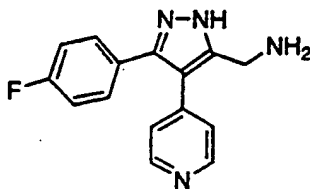
5

10

## Example C-1

15

## 5-AMINOMETHYL-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



20      1-(4-fluorophenyl)-2-(4-pyridyl)-1-ethanone.      4-  
picoline (40 g, 0.43 mol) was added to a LiHMDS solution  
(0.45 mol, 450 mL of a 1.0 M solution in THF) over 30  
minutes at room temperature (a slight exotherm was  
observed) The resulting solution was stirred for 1 h.  
25 This solution was added to ethyl 4-fluorobenzoate (75.8  
g, 0.45 mol, neat) over 1 h. The mixture was stirred  
overnight (16 h). Water (200 mL) was added and the  
mixture was extracted with EtOAc (2x200 mL). The organic  
layer was washed with brine (1x200 mL) and dried over

Na<sub>2</sub>SO<sub>4</sub>. The organic layer was filtered and the solvent was removed to leave oily solid. Hexane was added to the oil and the resulting solid was filtered and washed with hexane (cold). A yellow solid was isolated (50 g, 54%):  
5 <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.58 (d, J = 5.7 Hz, 2H), 8.02 (dd, J = 5.5, 8.0, 2H), 7.12-7.21 (m, 4H), 4.23 (s, 2H); <sup>19</sup>F NMR (CDCl<sub>3</sub>) δ -104.38 (m); LC/MS, t<sub>r</sub> = 2.14 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 216; High Resolution MS Calcd for  
10 C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>F (M+H): 216.0825. Found: 216.0830 (Δ mmu = 0.5).

**N-benzyloxycarbonyl-5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole.** A 3L round bottom flask  
15 fitted with a mechanical stirrer, N<sub>2</sub> inlet and an addition funnel was charged with 557 mL (0.56 mol) of 1 M t-BuOK in THF and 53 mL (0.56 mol) of t-BuOH. The ketone, 1 (60 g, 0.28 mol) was dissolved in 600 mL of THF and added to the stirred mixture at room temperature. A yellow  
20 precipitate formed and the mixture was stirred for 1 h. N-benzyloxycarbonyl-glyciny l N-hydroxysuccinimide (128.6 g, 0.42 mol) was dissolved in 600 mL of THF and added dropwise at r.t. over 1h. The mixture was stirred for another 5 minutes and 150 mL of water was added. the pH  
25 was adjusted to 6.7 with 70 mL of AcOH. Hydrazine monohydrate (41 mL in 100 mL of water) was added via an addition funnel. The mixture was stirred for 1 h and was diluted with 500 mL of water and 500 mL of ethyl acetate. The biphasic mixture was transferred to a sep funnel and  
30 the layers were separated. The aqueous layer was extracted with EtOAc (3x300 mL). The organic layer was

dried ( $\text{Na}_2\text{SO}_4$ ), filtered and evaporated to leave 157 g of a crude reddish oil.

The oil was suspended in  $\text{CH}_2\text{Cl}_2$  and filtered to remove any insoluble material (DCU, hydrazone of the monoketone). The solution was split into two portions and each portion was chromatographed (Biotage 75L, 3%  $\text{EtOH}/\text{CH}_2\text{Cl}_2$  then 6%  $\text{EtOH}/\text{CH}_2\text{Cl}_2$ ). The appropriate fractions were concentrated (some contamination from the monoketone and the hydrazone) from each portion to leave a yellow solid. The solid was suspended in ethyl acetate and heated to boiling for 10 minutes. The solution was allowed to cool to R.T. overnight. The precipitate was filtered to give 30 g of a white solid (27% yield of 2):  $^1\text{H}$  NMR ( $\text{DMF-d}_7$ )  $\delta$  13.36 (s, 1H), 8.57 (d,  $J = 5.8$  Hz, 2H), 7.16-7.52 (m, 11H), 5.11 (s, 2H), 4.48 (d,  $J = 5.4$  Hz, 2H);  $^{19}\text{F}$  NMR ( $\text{DMF-d}_7$ )  $\delta$  -114.9 (m), -116.8 (m) (split fluorine signal is due to the pyrazole tautomers); LC/MS,  $t_r = 3.52$  minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C),  $M+H = 403$ ; High Resolution MS Calcd for  $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{F}$  ( $M+H$ ): 403.1570. Found: 403.1581 ( $\Delta$  mmu = 1.1).

**5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl)**

**pyrazole.** To a 1L Parr bottle was added 7 g (17.4 mmol) of 2 and 180 mL of MeOH and 90 mL of THF to give a clear solution. The bottle was purged with nitrogen and 1.5 g of 10% Pd/C (wet Degussa type E101) was added. The Parr bottle was pressured to 40 psi ( $\text{H}_2$ ) and was agitated. Hydrogen uptake was 5 psi after 5 h. The bottle was repressured to 42 psi and was agitated overnight. The bottle was purged with  $\text{N}_2$  and was filtered through Celite. The Celite was washed with MeOH (3x50 mL) and

896

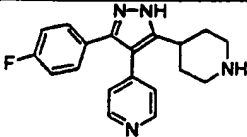
the filtrate was concentrated to give 4.5 g of an off-white solid (94%).  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  8.52 (d,  $J$  = 4.63 Hz, 2H), 7.36 (dd,  $J$  = 5.64, 8.1 Hz, 2H), 7.16-7.30 (m, 4H), 3.79 (s, 2H);  $^{19}\text{F}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  -114.56 (m); LC/MS,  $t_r$  = 1.21 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C),  $M+H$  = 269 m/z; High Resolution MS. Calcd for  $\text{C}_{15}\text{H}_{14}\text{N}_4\text{F}$  ( $M+H$ ): 269.1202. Found: 269.1229 ( $\Delta$  mmu = 2.7).

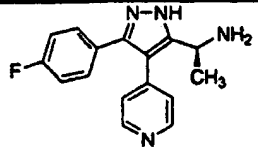
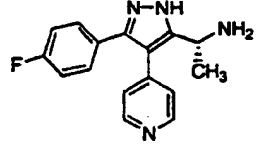
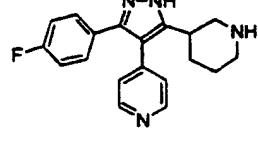
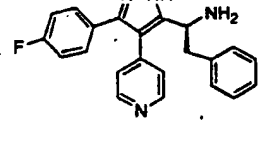
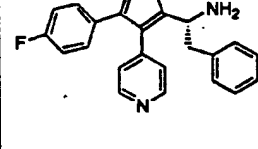
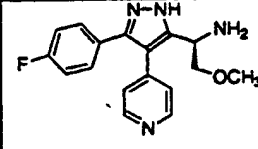
10

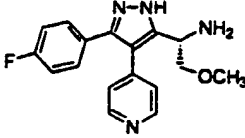
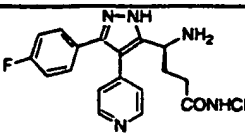
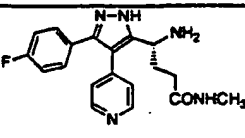
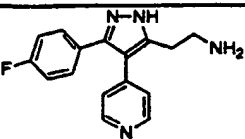
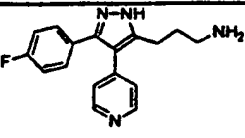
The following pyridylpyrazoles (C-2 through C-21, Table C-1) were prepared according to the experimental procedure described above for example C-1.

15

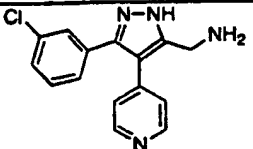
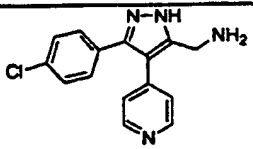
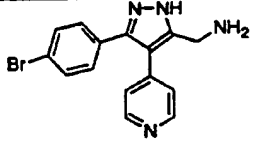
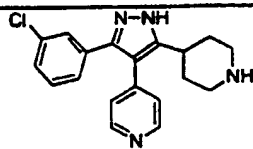
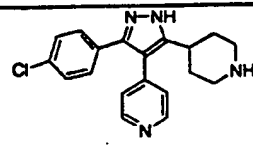
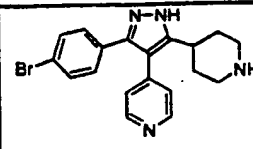
Table C-1.

Example No.	Structure	MW, $M + H$ Calculated Found	$^1\text{H}$ NMR (solvent), ppm
C-2		323.1672 323.1670	(DMF- $d_7$ ): 8.77 (t, $J$ = 4.4 Hz, 2H), 7.60 (m, 2H), 7.44 (t, $J$ = 4.4 Hz, 2H), 7.35 (m, 2H), 3.22 (bd, 2H), 3.01 (septet, $J$ = 5.3 Hz, 1H), 2.74 (m, 2H), 1.95 (m, 4H)

C-3		282.127 (M) 282.1245 (M, EI)	(DMF-d <sub>7</sub> ): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.34 (m, 2H), 4.40-4.37 (m, 1H), 1.56 (br s, 3H)
C-4		282.127 (M) 282.1147 (M, EI)	(DMF-d <sub>7</sub> ): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.35 (m, 2H), 4.40-4.37 (m, 1H), 1.57 (br s, 3H)
C-5		323.1672 323.1687	(DMSO-d <sub>6</sub> ): 8.56 (br, 2H), 7.32 (m, 2H), 7.18 (m, 4H), 2.91 (m, 2H), 2.71 (m, 2H) 1.88 (m, 1H), 1.65 (m, 2H), 1.40 (m, 2H)
C-6		359 359	(DMSO-d <sub>6</sub> ): 8.46 (d, J = 4.6 Hz, 2H), 7.32-7.13 (m, 7H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.95 (m, 2H)
C-7		359 359	(DMSO-d <sub>6</sub> ): 8.46 (d, J = 5.4 Hz, 2H), 7.32-7.28 (m, 2H), 7.20-7.12 (m, 5H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.94 (m, 2H)
C-8		313.1465 313.1492	(DMSO-d <sub>6</sub> ): 13.83 (bs, 1H), 8.61 (d, J = 5.7 Hz, 2H), 8.33 (bs, 1H), 7.33 (m, 6H), 4.44 (m, 1H), 3.63 (m, 2H), 3.27 (s, 3H)

C-9		313.1465 313.1457	(DMSO-d <sub>6</sub> ): 8.55 (dd, J = 1.5, 4.4 Hz, 2H), 7.37-7.32 (m, 2H), 7.26 (dd, J = 1.6, 4.4 Hz, 2H), 7.22-7.16 (m, 2H), 4.06 (t, J = 6.5 Hz, 1H), 3.49 (d, J = 6.6 Hz, 2H), 3.20 (s, 3H)
C-10		354 354	(DMSO-d <sub>6</sub> ): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-11		354 354	(DMSO-d <sub>6</sub> ): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-12		283.1359 283.1363	(DMSO-d <sub>6</sub> ): 8.53 (d, J = 5.0 Hz, 2H), 7.37-7.32 (m, 2H), 7.21-7.17 (m, 4H), 2.83 (d, J = 6.0 Hz, 2H), 2.77 (d, J = 6.0 Hz, 2H)
C-13		297.1515 297.1515	(DMSO-d <sub>6</sub> ): 8.53 (d, J = 5.4 Hz, 2H), 7.34 (dd, J = 5.8, 8.2 Hz, 2H), 7.18



			(dd, $J = 5.8, 9.8$ Hz, 4H), 2.68 (t, $J = 7.3$ Hz, 2H), 2.52 (m, 2H), 1.64 (m, 2H)
C-14		284.0829 284.0806	(CD <sub>3</sub> OD): 8.74 (br, 2H), 7.77 (br, 2H), 7.45-7.58 (m, 3H), 7.30-7.40 (m, 1H), 4.43 (s, 2H)
C-15		285 285	(DMSO-d <sub>6</sub> ): 8.53 (br, 2H), 7.56 (br, 2H), 7.26 (m, 4H), 3.75 (br, 2H)
C-16		329, 331 329, 331	(DMSO-d <sub>6</sub> ): 8.53 (d, $J =$ 4.4 Hz, 2H), 7.42 (d, $J =$ 7.9 Hz, 2H), 7.34 (d, $J =$ 8.5 Hz, 2H), 7.24 (d, $J =$ 4.6 Hz, 2H), 3.76 (bs, 2H)
C-17		339 339	(DMSO-d <sub>6</sub> ): 8.53 (t, $J =$ 4.3 Hz, 2H), 7.33 (m, 3H), 7.19 (t, $J = 4.6$ Hz, 2H), 7.14 (d, $J = 7.3$ Hz, 1H), 3.23 (m, 2H), 2.88 (m, 3H), 1.92 (m, 3H), 1.70 (m, 1H)
C-18		339 339	(DMSO-d <sub>6</sub> ): 8.57 (d, $J =$ 4.6 Hz, 2H), 7.41 (d, $J =$ 8.3 Hz, 2H), 7.29 (d, $J =$ 8.5 Hz, 2H), 7.20 (d, $J =$ 4.8 Hz, 2H), 3.18 (bd, 2H), 2.88 (m, 1H), 2.76 (m, 2H), 1.82 (br, 4H)
C-19		383, 385 383, 385	(DMSO-d <sub>6</sub> ): 8.56 (br, 2H), 7.52 (br, 2H), 7.14-7.29 (m, 4H), 2.99 (br, 2H),

900

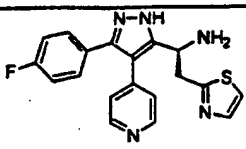
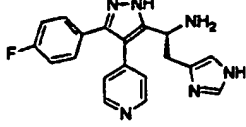
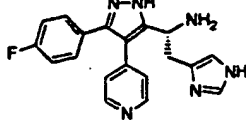
			2.71 (br, 1H), 2.51 (br, 2H), 1.68 (br, 4H)
--	--	--	---

5

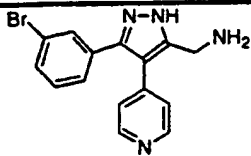
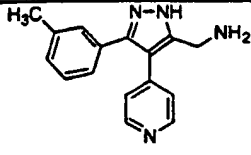
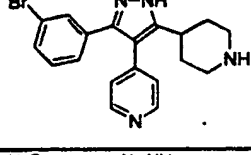
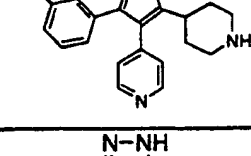
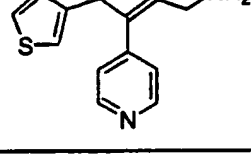
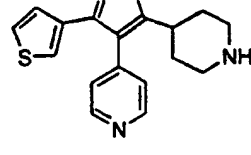
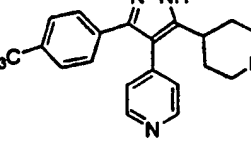
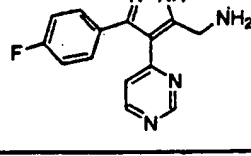
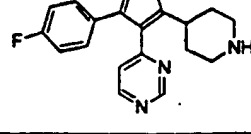
10

The following pyridylpyrazoles (C-22 through C-40, Table C-2) are prepared utilizing the general schemes C-1 and C-2 and the experimental procedure described for example C-1 above.

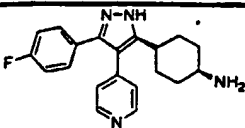
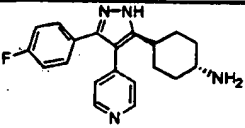
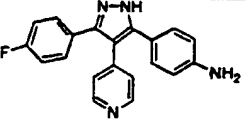
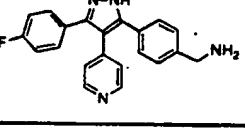
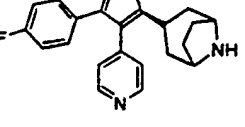
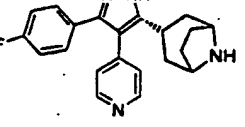
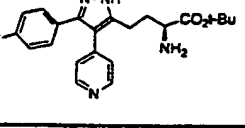
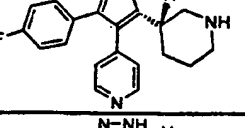
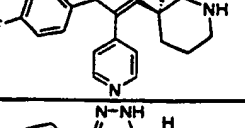
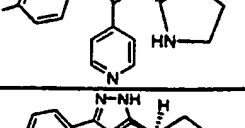
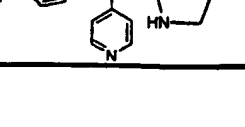
Table C-2

Cmpd. No.	Structure
C-22	
C-23	
C-24	

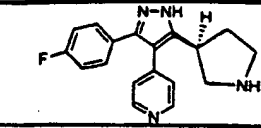
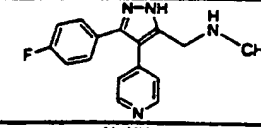
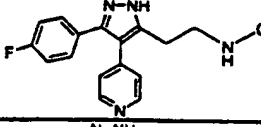
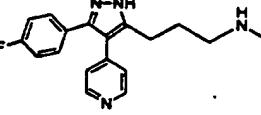
901

C-25	
C-26	
C-27	
C-28	
C-29	
C-30	
C-31	
C-32	
C-33	

902

C-34	
C-35	
C-36	
C-37	
C-38	
C-39	
C-40	
C-41	
C-42	
C-43	
C-44	

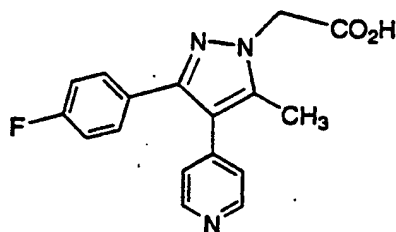
903

C-45	
C-46	
C-47	
C-48	

5

**Example C-49**

10



15

**Step A**

The pyrazole (2.60 g, 10.3 mmol) from **example C-4** was suspended in 52 mL of dichloroethane and 52 mL of 2.5 M

904

NaOH. Tetrabutylammonium hydroxide (0.5 mL of a 1 M aqueous solution) was added to the stirred mixture. To this mixture was added t-butyl bromoacetate (2.10 g, 10.8 mmol). The reaction mixture was stirred at room temperature for 4 h. The mixture was poured onto 200 mL of CH<sub>2</sub>Cl<sub>2</sub> and 200 mL of H<sub>2</sub>O. The phases were separated and the organic phase was washed with water (1x100 mL) and brine (1x100 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and was filtered. The solvent was removed to leave an off-white solid. This solid was triturated with hexane and the resulting solid isolated by filtration. The solid was washed with hexane to leave 3.4 g of a white solid (90%).

15

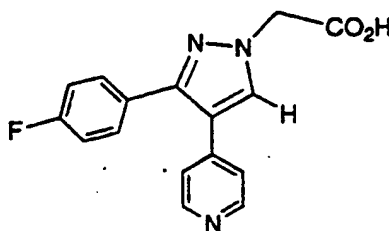
### Step B

The alkylated pyrazole (3.7 g, 10.1 mmol) from Step A was treated with 57 mL of 4 N HCL in dioxane. The solution was stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in THF. The solution was treated with propylene oxide (10.3 mmol) and was stirred for 1h at room temperature. The solvent was removed to leave an oil. The residual solvent was chased with several portions of EtOH. The resulting solid was triturated with Et<sub>2</sub>O and the title compound Example C-49 was isolated by filtration to afford 3.0 g of an off-white solid (95%). Mass spec: M+H calcd: 312; found 312. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): 8.81 (d, J = 6.4 Hz, 2H), 7.73 (d, J =

905

5.8 Hz, 2H), 7.40 (m, 2H), 7.23 (t, J = 8.5 Hz, 1H), 5.16 (s, 2H), 2.40 (s, 3H).

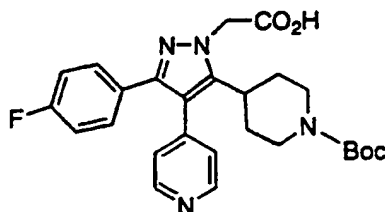
5

**Example C-50**

According to the procedure described above in Example C-  
10 49, Example C-50 was also prepared starting from 4-[3-(4-fluorophenyl)-1H-pyrazole-4-yl]pyridine. Mass spec: M+H  
calcd: 298; found 298. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): 8.75 (d, J =  
6.4 Hz, 2H), 8.68 (s, 1H), 7.78 (d, J = 6.6 Hz, 2H), 7.52  
(dd, J = 5.4, 8.5 Hz, 2H), 7.31 (t, J = 8.9 Hz, 2H),  
15 5.16 (s, 2H).

**Example C-51**

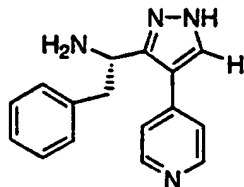
20



Starting with the N-Boc-piperidinyl analog of Example C-  
2, Example C-51 is also prepared according to the methods  
described in Scheme C-1.

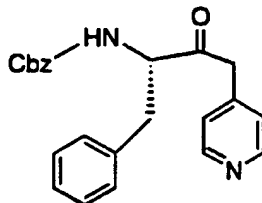
**Example C-52**

5



Step A: Picoline is treated with a base chosen from but not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH in an organic solvent such as THF, ether, t-BuOH or dioxane  
10 from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The picoline solution is then added to a solution of N-Cbz-(L)-phenylalaninyl N-hydroxysuccinimide. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature  
15 may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone is isolated as a crude solid which could be purified by crystallization and/or chromatography.

20

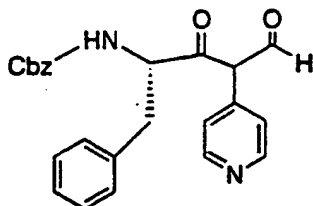


25 Step B: A solution of the pyridyl monoketone in ether, THF, tBuOH, or dioxane is added to a base chosen from but



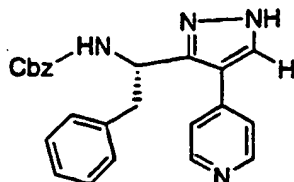
907

not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH contained in hexane, THF, ether, dioxane, or tBuOH from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. Formyl acetic anhydride is then added as a solution in THF, ether, or dioxane to the monoketone anion while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from 5 minutes to several hours. The resulting pyridyl diketone intermediate is utilized without purification in Step C.



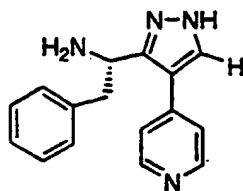
Step C: The solution containing the pyridyl diketone is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc, H<sub>2</sub>SO<sub>4</sub>, HCl, or HNO<sub>3</sub>. The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate is then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to several hours. The mixture is then poured into water and extracted with an organic solvent. The N-Cbz-protected pyridyl pyrazole is obtained as a crude solid which is purified by chromatography or crystallization.

908



## 5 Step: D

The CBZ protecting group is cleaved using hydrogen gas under pressure and Pd-C in an alcohol solvent, affording scaffold C-52 after filtration and concentration.

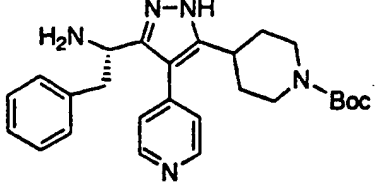
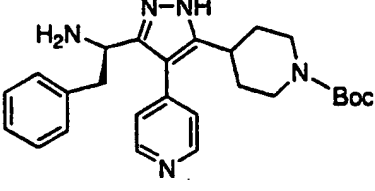
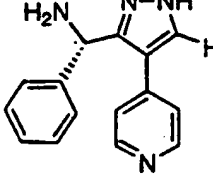
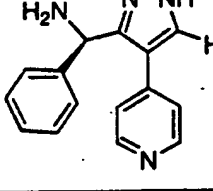
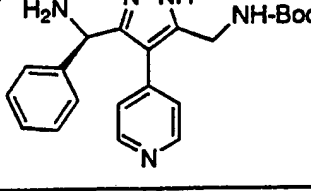
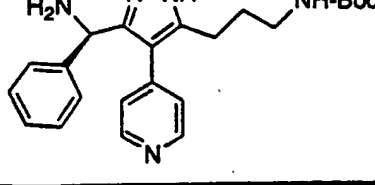


10

- 15 The following compounds C-53 through C-59 in Table C-3 are prepared according to the general procedure described above for the preparation of C-52.

Table C-3

Example No.	Structure
C-53	

C-54	
C-55	
C-56	
C-57	
C-58	
C-59	

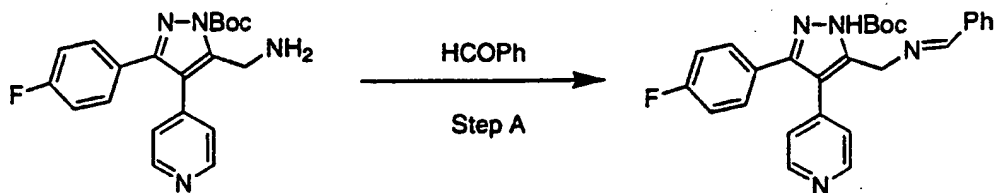
**Example C-60****5 Step A:**

A Boc protected pyridylpyrazole is treated with benzaldehyde in methylene chloride at room temperature in

910

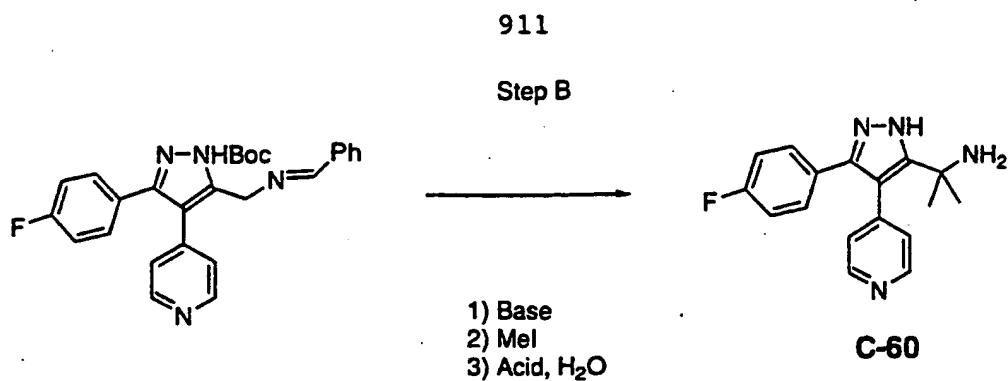
the presence of a drying agent for a period of time ranging from 1-24 h. Solvent is then evaporated and the resulting imine is used in step B without further purification.

5

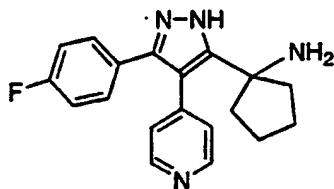


Step B:

The pyridylpyrazole imine is dissolved in THF and stirred  
10 under nitrogen at temperatures ranging from -78 to -20 °C.  
A base such as LDA, n-BuLi, or LiHMDS is added dropwise  
to the mixture which is then stirred for an additional 10  
minutes to 3 h. Two equivalents of a methyl iodide are  
then added to the mixture and stirring is continued for  
15 several hours. The mixture is then quenched with acid  
and allowed to warm to room temperature and stirred  
several hours until cleavage of the Boc and the imine  
functions is complete. The pH is adjusted to 12 and then  
the mixture is extracted with an organic solvent, which  
20 is dried and evaporated. The crude pyridylpyrazole is  
then crystallized and/or chromatographed to give purified  
C-60.



5

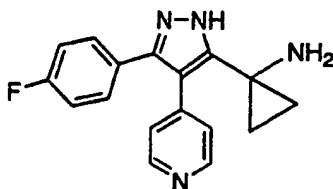
**Example C-61**

10 Example C-61 is prepared according to the method described in example C-60, substituting 1,4-dibromobutane for methyl iodide.

15

20

**Example C-62**



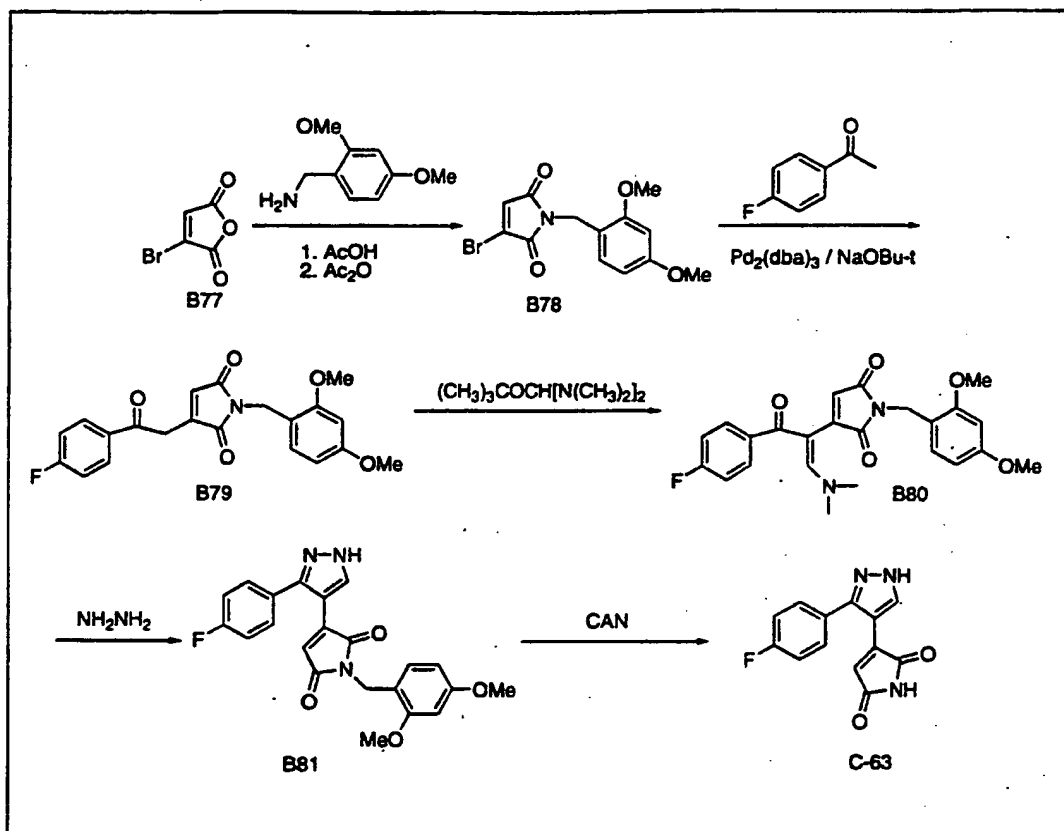
Example C-62 is prepared according to the method described in example C-60, substituting 1,3-dibromoethane for methyl iodide.

5

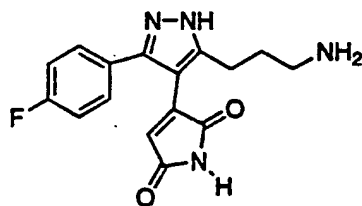
#### Example C-63

The synthesis of compound C-63 starts with the  
10 condensation reaction of bromomaleic anhydride B77 with  
2, 4-dimethoxybenzylamine in acetic acid and acetic  
anhydride. The maleimide B78 is then treated with 4'-  
fluoroacetophenone in the presence of catalytic amount  
Pd<sub>2</sub>(dba)<sub>3</sub> and sodium t-butoxide to form the  
15 fluoroacetophenone substituted maleimide B79. B79 is  
then treated with tert-butoxybis(dimethylamino)methane to  
yield the α-ketoenamine B80. The α-ketoenamine B80 is  
condensed with hydrazine to form the N-protected  
maleimide pyrazole B81. The 2,4-dimethoxybenzyl group is  
20 cleaved with ceric ammonium nitrate (CAN) to give the  
title compound C-63.

913

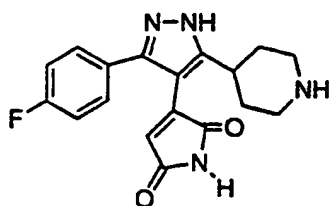
**Example C-64**

5



Using the method described in Schemes C-6 and C-7,  
10 Example 64 is prepared.

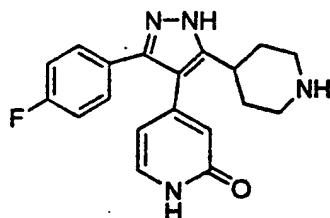
914

**Example C-65**

5

Using the method described in Schemes C-6 and C-7,  
Example 65 is prepared.

10

**Example C-66**

15

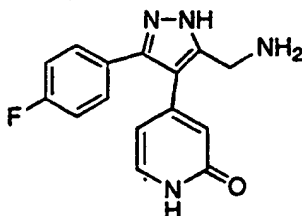
Using the method described in Schemes C-6 and C-7,  
Example C-66 is synthesized, substituting N-2,4-  
20 dimethoxybenzyl-4-bromopyridone for B78.

25



**Example C-67**

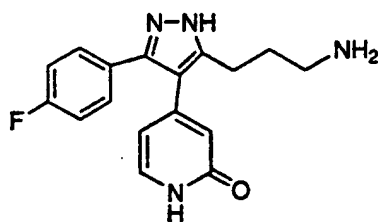
5



Using the method described in Schemes C-6 and C-7,  
Example C-67 is synthesized, substituting N-2,4-  
10 dimethoxybenzyl-4-bromopyridone for B78, and substituting  
N-Boc-glycyl N-hydroxysuccinimide for B82.

**Example C-68**

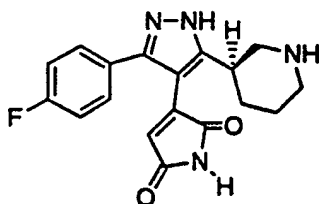
15



Using the method described in Schemes C-6 and C-7,  
20 Example C-68 is synthesized, substituting N-2,4-  
dimethoxybenzyl-4-bromopyridone for B78.

25

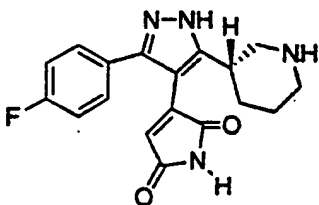
916

**Example C-69**

5

Using the method described in Schemes C-6 and C-7, Example 69 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

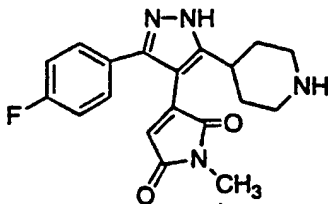
10

**Example C-70**

15 Using the method described in Schemes C-6 and C-7, Example 70 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

**Example C-71**

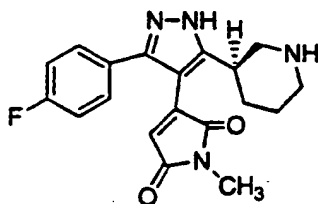
20



917

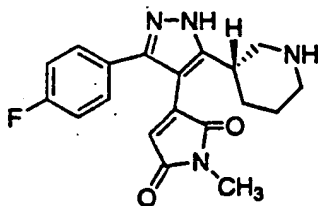
Using the method described in Schemes C-6 and C-7, Example 71 is prepared, substituting N-methyl-3-bromomaleimide for B78.

5

**Example C-72**

10 Using the method described in Schemes C-6 and C-7, Example 72 is prepared, substituting N-methyl-3-bromomaleimide for B78, and substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

15

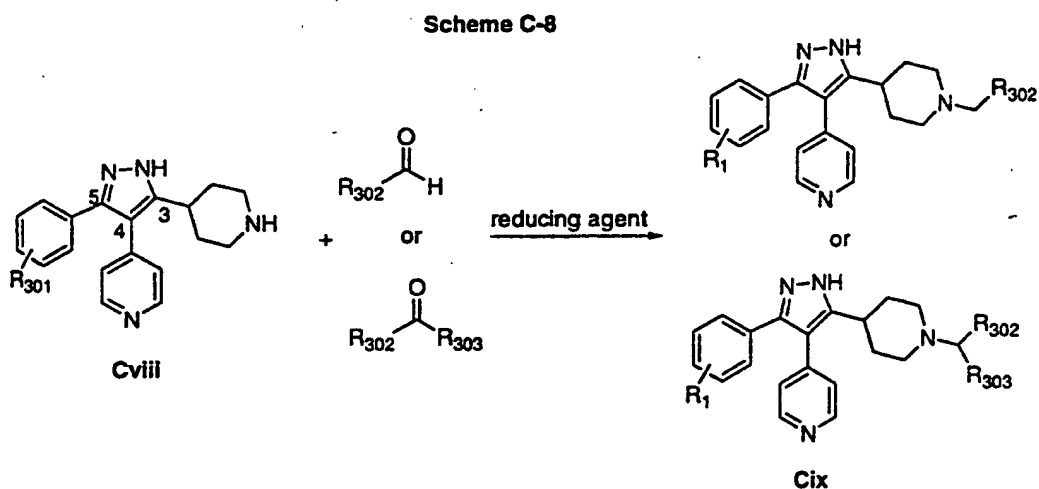
**Example C-73**

Using the method described in Schemes C-6 and C-7, Example 73 is prepared, substituting N-methyl-3-bromomaleimide for B78 and substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

25

## General Synthetic Procedures

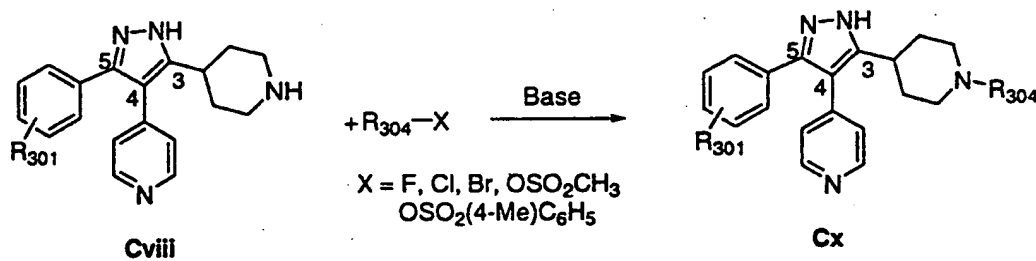
Scheme C-8 illustrates a general method that can be used for the introduction of various groups on an unsubstituted nitrogen atom that is present as part of pyrazole (Cviii) with appropriately substituted aldehydes ( $R_{302}CHO$ ) or ketones ( $R_{302}COR_{303}$ ) in the presence of a reducing agent such as sodium cyanoborohydride or sodium triacetoxyborohydride affords the desired products (Cix). Typical conditions for the reductive alkylation include the use of an alcoholic solvent at temperatures ranging from 20 °C to 80 °C. In Scheme C-8,  $R_{302}$  and  $R_{303}$  are selected from but not limited to alkyl, benzyl, substituted benzyl, arylalkyl, heteroarylalkyl.



Scheme C-9 illustrates another method for introduction of substituents on the unsubstituted nitrogen atom present as part of the C-3 position of the pyrazole (Cviii). Treatment of the pyrazole (Cviii) with

a suitable alkylating agent ( $R_{304}X$ ) such as an alkyl chloride, alkyl bromide, alkyl iodide or with an alkyl methanesulfonate or alkyl p-toluenesulfonate in the presence of a suitable base affords the desired alkylated pyrazoles (**Cx**). Examples of suitable bases include diisopropylethylamine, triethylamine, N-methylmorpholine, potassium carbonate and potassium bicarbonate.

Scheme C-9

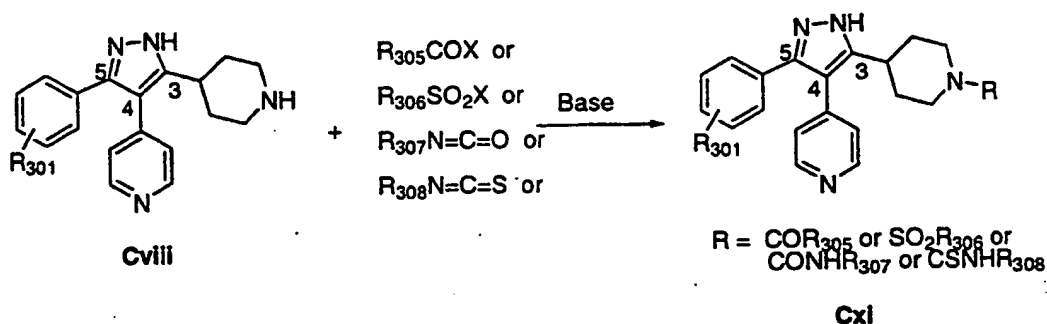


Typical conditions for the alkylation include reaction with the suitable base in a polar aprotic solvent such as acetonitrile, dimethylformamide, dimethylacetamide or dimethyl sulfoxide at temperatures ranging from 20 °C to 150 °C. Typical  $R_{304}$  substituents are selected from but are not limited to alkyl, substituted benzyl, heteroaromatic, substituted heteroalkyl and substituted heteroarylalkyl groups.

Compounds containing acyl, sulfonyl or ureidyl groups at the nitrogen atom can be prepared as shown in Scheme C-10. Treatment of the pyrazole **Cviii** with a suitable acylating agent in the presence of a base such as N-methylmorpholine, triethylamine, diisopropylethylamine or dimethylamino pyridine in an

organic solvent such as dichloromethane, dichloroethane or dimethylformamide at temperatures ranging from 20 °C to 120 °C affords the desired acylated pyrazoles (Cxi). Suitable acylating agents include acid halides, activated esters of acids such as the N-hydroxysuccinimide esters, p-nitrophenyl esters, pentafluorophenyl esters, sulfonyl halides, isocyanates, and isothiocyanates.

Scheme C-10



A general synthesis of 2-substituted pyrimidinylpyrazole compounds of type Cxv is shown in Scheme C-11.

#### Step A:

4-Methyl-2-methylmercaptopyrimidine is treated with a base selected from but not limited to n-BuLi, LDA, LiHMDS, t-BuOK, NaH in an organic solvent such as THF, ether, t-BuOH, dioxane from -78 °C to 50 °C for a period of time from 30 minutes to 5 hours. The resulting 4-methyl anion is then added to a solution of an appropriate ester B88. The reaction is allowed to stir from 30 minutes to 48 hours during which time the

temperature may range from 0 °C to 100 °C. The reaction mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the desired monoketone **B89** is isolated as a crude solid which can be recrystallized or purified by chromatography.

Step B:

Monoketone **B89** is treated with a base selected from but not limited to n-BuLi, LDA, LiHMDS, t-BuOK, NaH, K<sub>2</sub>CO<sub>3</sub> or Cs<sub>2</sub>CO<sub>3</sub> in an organic solvent such as THF, ether, t-BuOH, dioxane, toluene or DMF from -78 °C to 50 °C for a period of time from 30 minutes to 5 hours. A solution of an appropriately activated ester of a carboxylic acid  $\text{CbzNR}^n-(\text{CH}_2)_n\text{CR}^f(\text{R}^g)-\text{COOH}$  or  $\text{BocNR}^n-(\text{CH}_2)_n\text{CR}^f(\text{R}^g)-\text{COOH}$ , preferably but not limited to the N-hydroxysuccinimide ester **B90** is then added to the monoketone anion while maintaining the temperature between 0 °C to 100 °C. The reaction is allowed to stir at the specified temperature for a period of time ranging from 30 minutes to 48 hours. The resulting pyrimidine diketone intermediate **B91** is utilized without further purification in Step C.

Step C:

The solution or suspension containing the diketone intermediate **B91** is quenched with water and the pH adjusted to between 4 and 8 using an acid chosen from AcOH, H<sub>2</sub>SO<sub>4</sub>, HCl or HNO<sub>3</sub> while maintaining the temperature between 0 °C to 40 °C. Hydrazine or hydrazine monohydrate is then added to the mixture while maintaining the temperature between 0 °C to 40 °C. The mixture is stirred

for a period of 30 minutes to 16 hours maintaining the temperature between 20 °C to 50 °C, poured into water and extracted with an organic solvent. The pyrimidinyl pyrazole **CxiiBoc** or **CxiiCbz** is obtained as crude solid which is purified by chromatography or crystallization.

Step D:

The 2-methylmercapto group in the pyrimidinyl pyrazole (**CxiiBoc** or **CxiiCbz**) is oxidized to the 2-methylsulfone (where  $n = 2$ ) or the 2-methylsulfoxide (where  $n = 1$ ) using either Oxone or m-chloroperbenzoic acid as an oxidizing agent in a suitable solvent at temperatures ranging from 25 °C to 100 °C. Solvents of choice for the oxidation include dichloromethane, acetonitrile, tetrahydrofuran or hydroalcoholic mixtures. The 2-methylsulfone ( $n = 2$ ) or the 2-methylsulfoxide ( $n = 1$ ) (**CxiiiBoc** or **CxiiiCbz**) is purified by crystallization or chromatography.

Step E:

The 2-methylsulfone/2-methylsulfoxide group in **CxiiiBoc** or **CxiiiCbz** is conveniently displaced with various amines or alkoxides at temperatures ranging from 20 °C to 200 °C in solvents that include but are not limited to dimethylformamide, acetonitrile, tetrahydrofuran and dioxane. The alkoxides can be generated from their alcohols by treatment with a base selected from but not limited to sodium hydride, lithium hexamethyldisilazide, potassium tertiary-butoxide in solvents such as tetrahydrofuran, dimethylformamide and

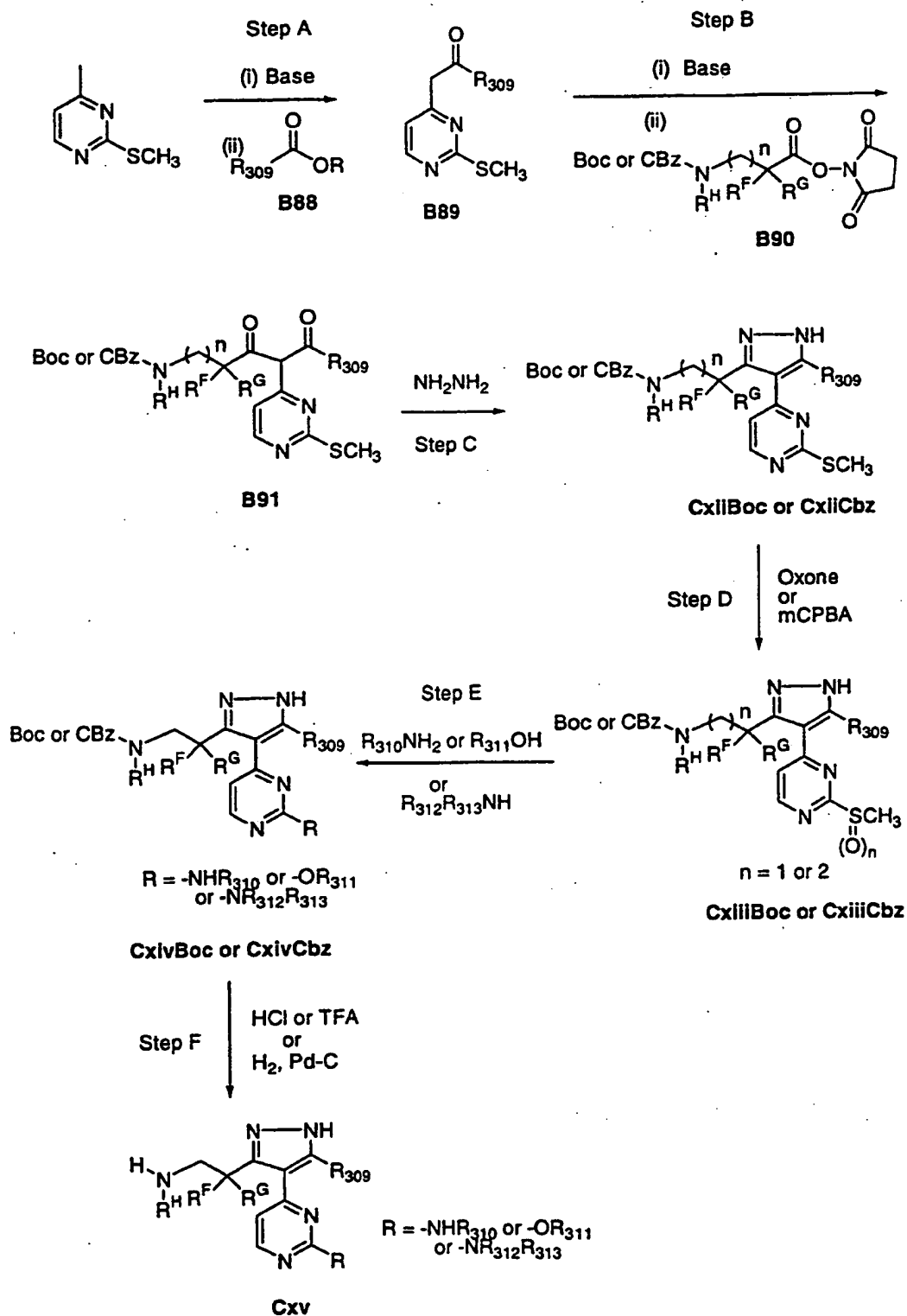


dioxane at temperatures ranging from 0 °C to 100 °C. The resulting 2-amino or 2-oxo derivatives (**CxivBoc** or **CxivCbz**) are purified by either chromatography or crystallization.

Step F:

The carbamate protecting groups from **CxivBoc** or **CxivCbz** are removed to afford the desired compounds **Cxv** containing either a free primary amine ( $R^H$  is hydrogen) or a free secondary amine ( $R^H$  is not equal to hydrogen). The Boc protecting groups are cleaved utilizing either trifluoroacetic acid in methylene chloride or hydrochloric acid in dioxane at room temperature for several hours. The Cbz protecting groups are cleaved using hydrogen gas at atmospheric or higher pressures and a catalyst (palladium on charcoal) in an alcoholic solvent. The resulting amines **Cxv** are then crystallized or purified by chromatography.

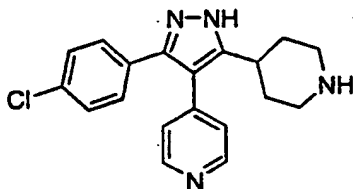
## SCHEME C-11



The following examples contain detailed descriptions of the methods of preparation of compounds that form part of the invention. These descriptions are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All compounds showed NMR spectra consistent with their assigned structures.

**Example C-74**

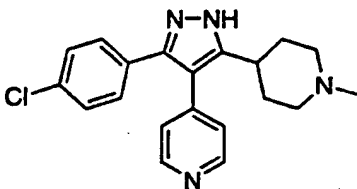
**5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



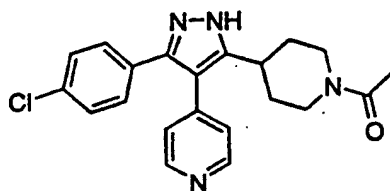
By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: <sup>1</sup>HNMR (d<sub>6</sub>-DMSO) δ 8.57 (d, *J* = 4.83 Hz, 2 H), 7.41 (d, *J* = 8.26 Hz, 2 H), 7.29 (d, *J* = 8.26 Hz, 2 H), 7.20 (d, *J* = 4.63 Hz, 2 H), 3.18 (bd, *J* =

926

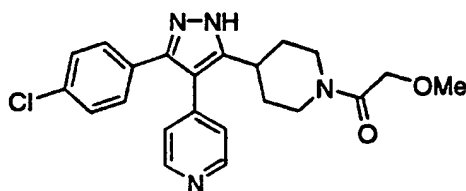
12.08 Hz, 2 H), 2.88 (m, 1 H), 2.76 (m, 2 H), 1.82 (bs, 4 H). MS (M+H): 339 (base peak).

**Example C-75****5-(N-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

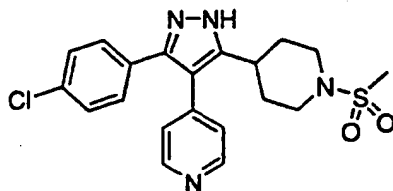
To a solution of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (25 g, 61 mmol) in 140 mL of formic acid (96%) was added 50 g of formaldehyde (37%). The solution was stirred at 75 °C for 48 h and was cooled to room temperature. The excess formic acid was removed under reduced pressure and the residue was dissolved in 100 mL of water. The solution was added to concentrated  $\text{NH}_4\text{OH}/\text{H}_2\text{O}$  and the mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine (1 x 250 mL) and was dried over  $\text{Na}_2\text{SO}_4$ . The solution was filtered and concentrated to leave a white solid. The solid was triturated with ether and was filtered to afford the title compound: MS (M+H): 353 (base peak).

**Example C-76****5-(N-ACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (1 g, 2.4 mmol) in 24 mL of  $\text{CH}_2\text{Cl}_2$ , was added 4-dimethylamino pyridine (0.88 g, 7.2 mmol) and acetyl chloride (0.21 g, 2.6 mmol). The solution was stirred for 3 h and the solvent was removed under reduced pressure. The residue was treated with saturated  $\text{NH}_4\text{OH}$  (20 mL) and the suspension was extracted with ethyl acetate (3 x 30 mL). The combined extracts were washed with brine (1 x 50 mL), dried over  $\text{MgSO}_4$ , filtered and concentrated to leave a solid. The solid was triturated with ether and was filtered to leave the title compound: MS (M+H): 381 (base peak).

**Example C-77****5-(N-METHOXYACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

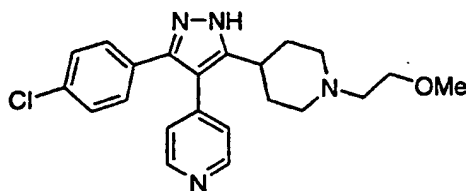
By following the method of Example C-76 and substituting methoxy acetyl chloride for acetyl chloride the title compound was prepared: <sup>1</sup>HNMR (DMSO-d<sub>6</sub>) δ 8.75 (d, J = 6.72 Hz, 2 H), 7.70 (d, J = 6.72 Hz, 2 H), 7.38 (d, J = 8.60 Hz, 2 H), 7.29 (dd, J = 6.72, 1.88 Hz, 2 H), 4.40 (d, J = 11.8 Hz, 1 H), 4.05 (m, 2 H), 3.70 (d, J = 12.70 Hz, 1 H), 3.25 (s, 3 H), 3.0 (m, 2 H), 2.55 (m, 1 H), 1.7 (m, 4 H). MS (M+H): 411 (base peak).

**Example C-78****5-(N-METHYLSULFONYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

By following the method of Example C-76 and substituting methylsulfonyl chloride (2.0 equivalents) for acetyl chloride the title compound was prepared: <sup>1</sup>HNMR (DMSO-*d*<sub>6</sub>) δ 8.70 (d, *J* = 6.72 Hz, 2 H), 7.72 (d, *J* = 6.72 Hz, 2 H), 7.38 (d, *J* = 7.66 Hz, 2 H), 7.30 (dd, *J* = 6.72, 1.88 Hz, 2 H), 3.58 (bd, *J* = 11.8 Hz, 2 H), 2.87 (m, 1 H), 2.82 (s, 3 H), 2.72 (m, 2 H), 1.85 (m, 4 H). MS (M+H): 417 (base peak).

#### Example C-79

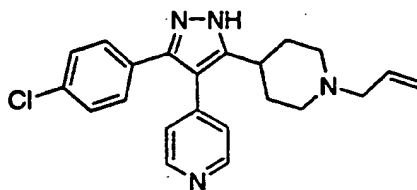
#### 5-[N-METHOXYETHYL-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (500 mg, 1.2 mmol) in 12 mL of DMF was added Hunig's base (790 mg, 6.1 mmol) and 2-bromoethyl methyl ether (850 mg, 6.1 mmol). The solution was stirred at room temperature for 5 days. The solution was poured onto 2.5 N NaOH and was extracted with ethyl acetate (3 x 100 mL). The combined extracts were washed with water (3 x 100 mL) and brine (1 x 100 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and was filtered. The

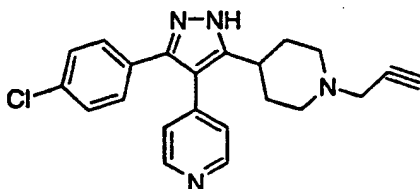
930

solvent was removed under reduced pressure to leave a solid. The solid was triturated and filtered to leave the title compound: <sup>1</sup>HNMR (CDCl<sub>3</sub>) δ 8.63 (d, *J* = 4.23 Hz, 2 H), 7.28 (m, 4 H), 7.14 (d, *J* = 4.43 Hz, 2 H), 3.57 (t, *J* = 5.24 Hz, 2 H), 3.38 (s, 3 H), 3.14 (bd, *J* = 10.1 Hz, 2 H), 2.79 (m, 1 H), 2.68 (t, *J* = 5.04, 2 H), 2.08 (m, 4 H), 1.92 (m, 2 H). MS (M+H): 397 (base peak).

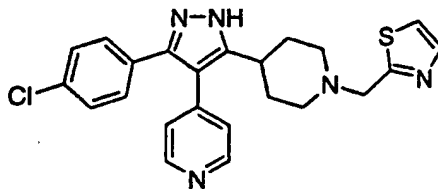
**Example C-80****5-(N-ALLYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

By following the method of example C-79 and substituting allyl bromide for 2-bromoethyl methyl ether the title compound was prepared: MS (M+H): 379 (base peak)



**Example C-81****5-(N-PROPARGYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

By following the method of example C-79 and substituting propargyl bromide for 2-bromoethyl methyl ether the title compound was prepared: MS (M+H): 377 (base peak)

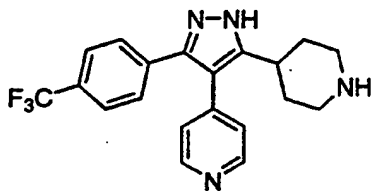
**Example C-82****5-[N-(2-METHYLTHIAZOLYL)-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

To a suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) in 12 mL of MeOH was added trimethyl orthoformate (2.6 g,

24.4 mmol) and 2-thiazolecarboxaldehyde (1.4 g, 12.2 mmol). The suspension was stirred at room temperature for 2 h. To this mixture was added NaCNBH<sub>3</sub> (1.5 g, 24.4 mmol) and the resulting suspension was stirred at room temperature for 7 days. The mixture was poured onto 2.5 N NaOH and was extracted with ethyl acetate (2 x 100 mL). The combined extracts were washed with brine (1 x 100 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to leave a solid. This solid was triturated with ether and filtered to afford the title compound: MS (M+H): 436 (base peak).

#### Example C-83

#### 5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



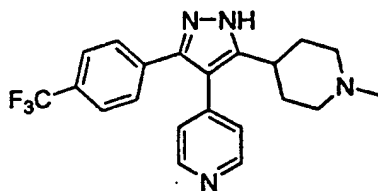
By following the method of Example C-1 and substituting methyl-4-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate

933

was accomplished with 4 N HCl in dioxane to afford the title compound as its hydrochloride salt: MS (M+H): 373 (base peak).

**Example C-84**

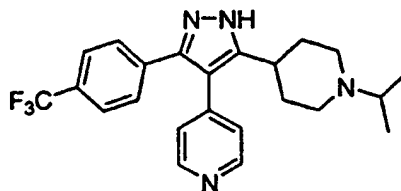
**5-(N-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole hydrochloride (Example C-83) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 387 (base peak).

**Example C-85**

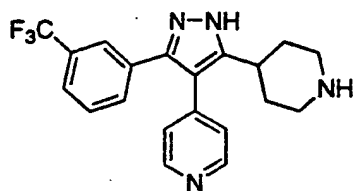
**5-[N-(2-PROPYL)-4-PIPERIDYL]-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



To a solution of 5-(4-piperidyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole (Example C-83) (300 mg, 0.7 mmol) in 50 mL of acetone was added 1 mL of AcOH and NaBH(OAc)<sub>3</sub> (15 g, 70.8 mmol). The mixture was warmed to reflux and was stirred for 5 days. The reaction mixture was poured onto 100 mL of 2.5 N NaOH and was extracted with ethyl acetate (2 x 100 mL). The extracts were combined and washed with brine (1 x 100 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated to afford the title compound: MS (M+H): 415 (base peak).

#### Example C-86

#### 5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



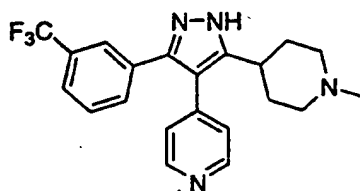
By following the method of Example C-1 and substituting methyl-3-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the

935

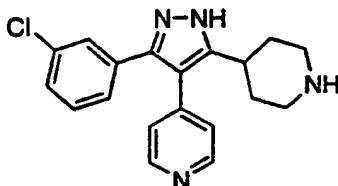
title compound as its hydrochloride salt: MS (M+H): 373  
(base peak).the pyrazole C-3 substituent (Cviii).  
Treatment of the

**Example C-87**

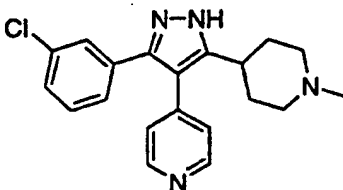
**5-(N-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-[3-(trifluoromethyl)phenyl] pyrazole hydrochloride (Example C-86) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 387 (base peak).

**Example C-88****5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE**

By following the method of Example C-1 and substituting methyl-3-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 339 (base peak).

**Example C-89****5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE**

937

By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(3-chlorophenyl) pyrazole hydrochloride (Example C-88) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 353 (base peak).

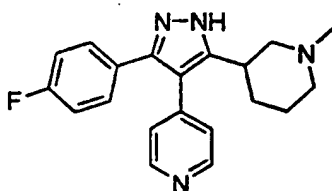
**Example C-90****5-(3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-nipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glyciny *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as its hydrochloride salt: MS (M+H): 323 (base peak).

938

**Example C-91**

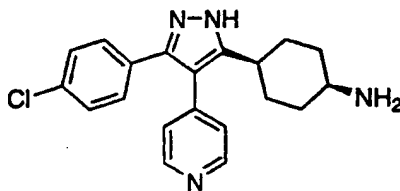
**5-(N-METHYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE**



By following the method of Example C-75 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole hydrochloride (Example C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 337 (base peak)..

**Example C-92**

**5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-  
CHLOROPHENYL) PYRAZOLE**



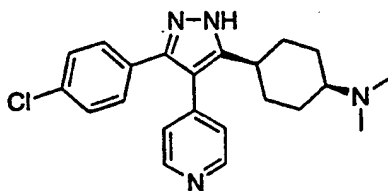
By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-



fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: <sup>1</sup>HNMR (d<sub>6</sub>-DMSO) δ 8.56 (d, *J* = 6.04 Hz, 2 H), 7.39 (d, *J* = 8.66 Hz, 2 H), 7.31 (d, *J* = 8.46 Hz, 2 H), 7.17 (d, *J* = 5.84 Hz, 2 H), 3.05 (m, 1 H), 2.62 (m, 1 H), 1.99 (m, 2 H), 1.53 (m, 6 H). MS (M+H): 353 (base peak).

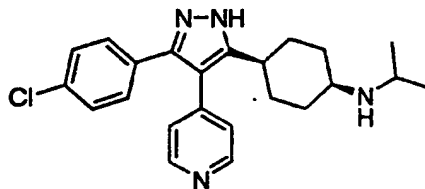
#### Example C-93

**5-*cis*-(4-*N,N*-DIMETYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 381 (base peak).

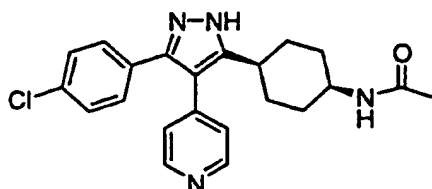
## Example C-94

**5-[*cis*-4-*N*-(2-PROPYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

To a slurry of 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) (1.0 g, 2.8 mmol, 1.0 eq) in methylene chloride (28 mL) was added acetone (0.5 mL), acetic acid (0.5 mL) and solid sodium triacetoxyborohydride. The slurry was stirred for 5 h and the volatiles were removed. The residue was partitioned between 2.5 M NaOH (25 mL) and ethyl acetate (25 mL) and the aqueous layer was extracted with ethyl acetate (3 x 25 mL). The combined organic layer was washed with brine (50 mL), dried over MgSO<sub>4</sub> and evaporated. The residue was triturated with ether to yield the title compound as a white powder: <sup>1</sup>H NMR (d<sub>6</sub>-DMSO) δ 8.56 (d, *J* = 5.84 Hz, 2H), 7.40 (d, *J* = 8.26 Hz, 2H), 7.30 (d, *J* = 8.66 Hz, 2H), 7.18 (d, *J* = 5.64 Hz, 2H), 2.95 (m, 2H), 2.72 (m, 1H), 1.90 (m, 2H), 1.73 (m, 2H), 1.55 (m, 4H), 1.07 (d, *J* = 5.64 Hz, 6H). MS (M+H): 395 (base peak).

**Example C-95**

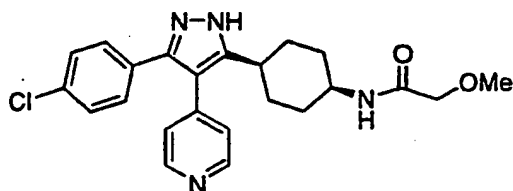
**5-*cis*-[4-*N*-(ACETYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 395 (base peak).

**Example C-96**

**5-*cis*-[4-*N*-(METHOXYACETYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



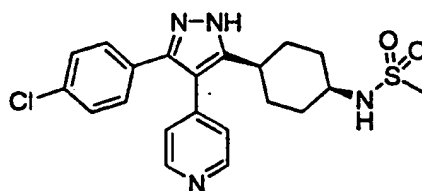
By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-

942

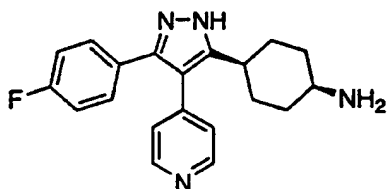
(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) and methoxy acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 425 (base peak).

#### Example C-97

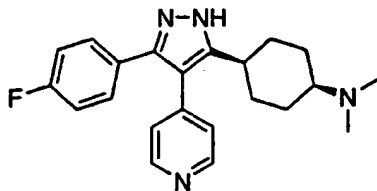
**5-*cis*-[4-*N*-(METHYLSULFONYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) and methanesulfonyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 431 (base peak).

**Example C-98****5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

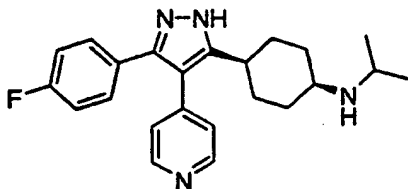
By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glyciny l *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 337 (base peak).

**Example C-99****5-(*cis*-4-*N,N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-98) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 365 (base peak).

**Example C-100**

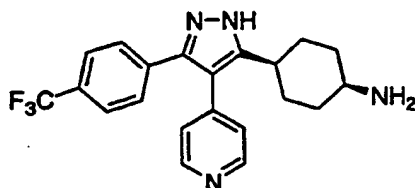
**5-*cis*-[4-*N*-(2-PROPYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**



By following the method of Example C-94 and substituting *cis*-5-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-98) for 5-(*cis*-4-*N*-(2-propyl)aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) the title compound was prepared: MS (M+H): 379 (base peak).

**Example C-101**

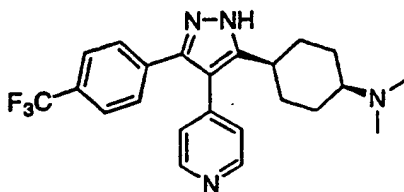
**5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



By following the method of Example C-1 and substituting methyl-4-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 387 (base peak).

**Example C-102**

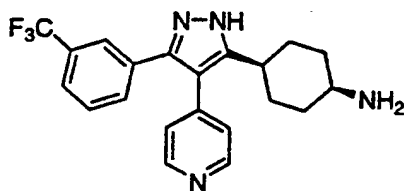
**5-*cis*-(4-*N,N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole (Example C-101) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 415 (base peak).

#### Example C-103

5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE

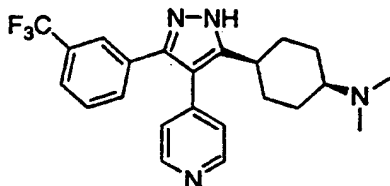


By following the method of Example C-1 and substituting methyl-3-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 387 (base peak).



## Example C-104

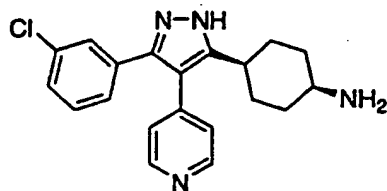
**5-*cis*-(4-*N,N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE**



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(3-(trifluoromethyl)phenyl) pyrazole (Example C-103) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 415 (base peak).

## Example C-105

**5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE**

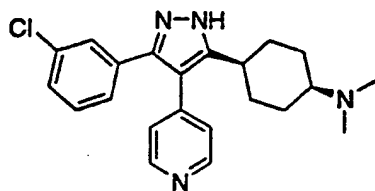


By following the method of Example C-1 and substituting methyl-3-chlorobenzoate for ethyl-4-

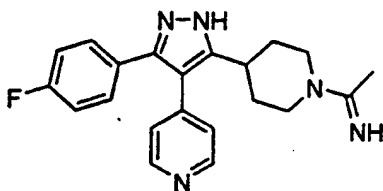
fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 353 (base peak).

#### Example C-106

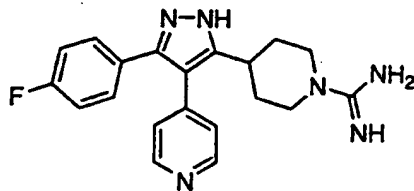
**5-*cis*-(4-*N,N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(3-chlorophenyl) pyrazole hydrochloride (Example C-105) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 381 (base peak).

**Example C-107****5-(N-ACETIMIDO-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

To a suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) (0.11 g, 0.35 mmol) in 2 mL EtOH was added ethyl acetamidate hydrochloride (0.065 g, 0.53 mmol) and the mixture was refluxed for 30 minutes. The solution was left at 5-10 °C for 16 h and filtered to obtain the title compound as a white solid: MS (M+H): 364 (base peak).

**Example C-108****5-(N-CARBOXAMIDINO-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

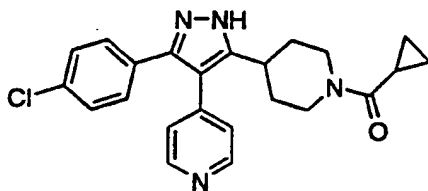
To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-2) (1.5 g, 4.7

950

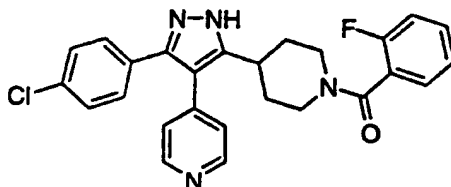
mmol) in 47 mL of DMF was added Hunig's base (0.60 g, 4.7 mmol) and pyrazole carboxamide hydrochloride (0.68 g, 4.7 mmol). The slurry was allowed to stir at room temperature for 4 days. The reaction mixture was poured onto 300 mL of ether. The resulting precipitate was filtered to leave the title compound as the hydrochloride salt: MS (M+H): 365 (base peak).

**Example C-109**

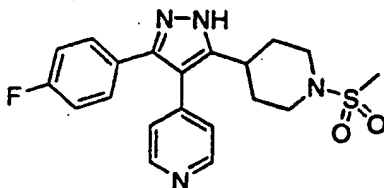
**5-(N-CYCLOPROPANOYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-76 and substituting cyclopropanoyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 407 (base peak).

**Example C-110****5-[N-(2-FLUORO)BENZOYL-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

By following the method of Example C-76 and substituting 2-fluorobenzoyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 461 (base peak).

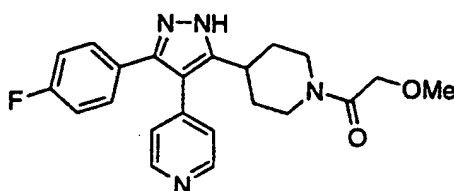
**Example C-111****5-(N-METHYLSULFONYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-74)

and methylsulfonyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 401 (base peak).

**Example C-112**

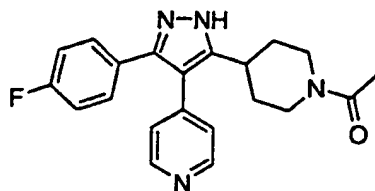
**5-(N-METHOXYACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**



By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-74) and methoxy acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 395 (base peak).

**Example C-113**

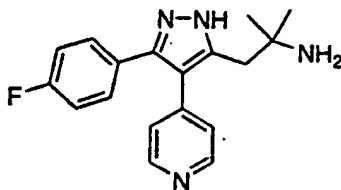
**5-(N-ACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**



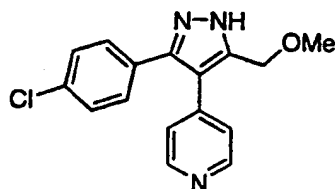
By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole Example (C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole Example (C-74) the title compound was prepared: MS (M+H): 365 (base peak).

**Example C-114**

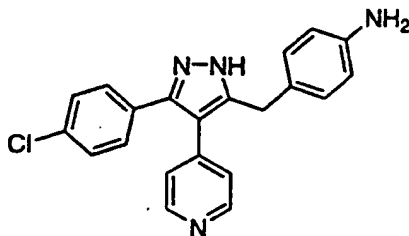
**5-[2-(1,1-DIMETHYL)AMINOETHYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**



By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-2-amino-2,2-dimethylpropanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: MS (M+H): 327 (base peak).

**Example C-115****5-(METHOXYMETHYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and 2-methoxyacetyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glyciny *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 300 (base peak).

**Example C-116****5-(4-AMINOBENZYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-4-aminophenyl

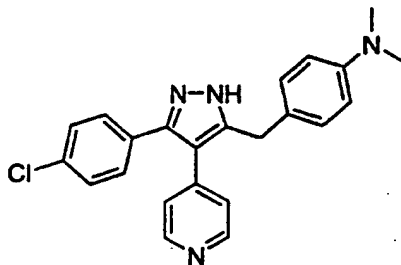


955

acetyl *N*-hydroxysuccinimide for *N*-benzyloxycarbonyl-glyciny *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 *N* HCl in dioxane to afford the title compound as the hydrochloride salt: MS (M+H): 361 (base peak).

**Example C-117**

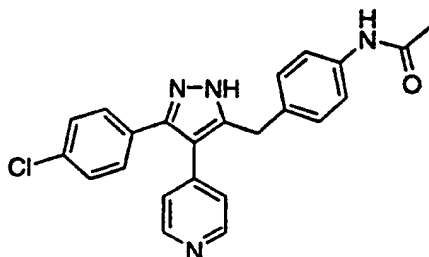
**5-[4-(*N,N*-DIMETHYL)AMINO BENZYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-75 and substituting 5-(4-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-116) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 389 (base peak).

## Example C-118

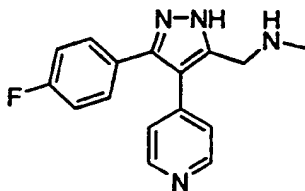
5-[4-(*N*-ACETYL)AMINO BENZYL]-4-(4-PYRIDYL)-3-(4-  
CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-(4-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-116) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 403 (base peak).

## Example C-119

5-(*N*-METHYLAMINOMETHYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE



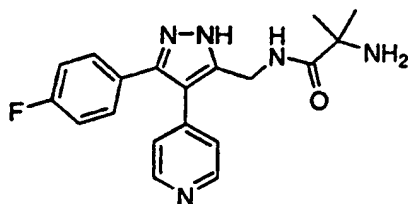
5-(*N*-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a suspension of 5-aminomethyl-

4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) (8.04 g, 30 mmol) in 120 mL dichloromethane was added p-nitrophenylformate (6.01 g, 36 mmol) as a solid. The suspension was stirred for 24 h at room temperature and the solvents removed under reduced pressure. The residue was triturated with ether and filtered to obtain the desired 5-(N-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole derivative as a white solid: MS (M+H): 297 (base peak).

5-(N-methylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a suspension of 5-(N-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (8.74 g, 29.5 mmol) in 90 mL anhydrous tetrahydrofuran was added a 1.0 M solution of borane in tetrahydrofuran (90 mL, 90 mmol) and the mixture was stirred at room temperature for 24 h. 1 N aqueous hydrochloric acid (100 mL) was then added to this mixture and the solution was refluxed for 5 hours and cooled to room temperature. The solution was extracted with ether (2 x 250 mL) and the pH of the aqueous layer adjusted to 9 by addition of concentrated ammonium hydroxide. The aqueous layers (pH ~ 9) were then extracted with ethyl acetate (4 x 150 mL). The organic extracts were dried over sodium sulfate, filtered and evaporated to dryness under reduced pressure. The residue was triturated with acetonitrile and filtered to obtain the title compound as a white solid: MS (M+H): 283 (base peak).

## Example C-120

## 5-[N-(2-AMINO-2,2-DIMETHYLACETYL)AMINOMETHYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



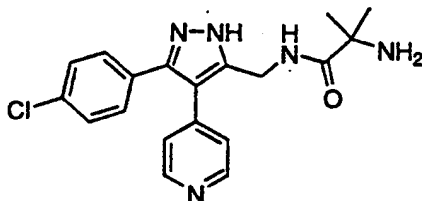
5-(*N*-*t*-butoxycarbonylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a solution of 5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) (0.27 g, 1 mmol) in anhydrous dimethylformamide (4 mL) was added *N*-tert-butoxycarbonyl aminoisobutyric acid *N*-hydroxysuccinimide ester (0.33 g, 1.1 mmol) and the mixture stirred at 40 °C for 24 h. The resulting solution was evaporated to dryness under reduced pressure. The residue was dissolved in dichloromethane (30 mL) and washed with a saturated solution of sodium bicarbonate (2 x 20 mL) and brine (20 mL). The organic layers were dried over sodium sulfate, filtered and evaporated under reduced pressure to dryness to afford 5-(*N*-*t*-butoxycarbonylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole as a white solid.

5-(*N*-(2-amino-2,2-dimethylacetyl)aminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a solution of the above compound in acetonitrile (2 mL) was added 1 mL of a 4.0 M solution of hydrochloric acid in dioxane. The

reaction mixture was stirred at room temperature for 6 hours. The suspension was evaporated to dryness under reduced pressure. The resulting residue was stirred in acetonitrile (5 mL), filtered and dried in a vacuum dessicator to afford the title compound as a hydrochloride salt: MS (M+H): 354 (base peak).

**Example C-121**

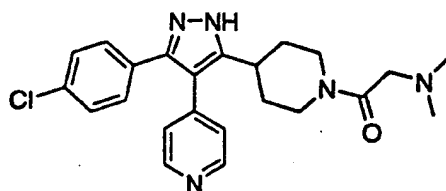
**5-[N-(2-AMINO-2,2-DIMETHYLACETYL)AMINOMETHYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**



By following the method of Example C-120 and substituting 5-aminomethyl-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-15) for 5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) the title compound was prepared: MS (M+H): 370 (base peak).

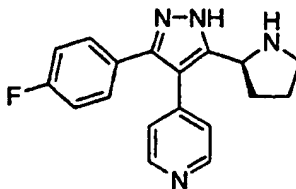
## Example C-122

5-[4-N-(2-DIMETHYLAMINOACETYL)PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

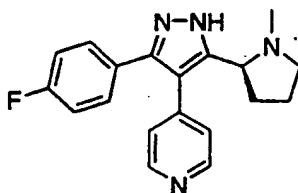


To a solution of N,N-dimethylglycine hydrochloride (0.28 g, 2 mmol) in dimethylformamide (4 mL) was added hydroxybenzotriazole (0.27 g, 2 mmol), N,N-diisopropylethyl amine (0.7 mL, 4 mmol) and polymer supported ethyl carbodimide (Example B-49) (1 g, 2.39 mmol). To this solution after 30 minutes at room temperature was added 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74), 0.41 g, 1 mmol). The suspension was agitated on a labtop orbital shaker for 24 h. The suspension was filtered, washed with dimethylformamide (2 x 5 mL) and the filtrates evaporated under high pressure. The residue was dissolved in dichloromethane (30 mL), washed with a saturated solution of sodium bicarbonate (50 mL) and brine (50 mL). The organic layers were dried over sodium sulfate, filtered and evaporated under high vacuum to afford the title compound as a white solid: MS (M+H): 424 (base peak).

961

**Example C-123****(S)-5-(2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)****PYRAZOLE**

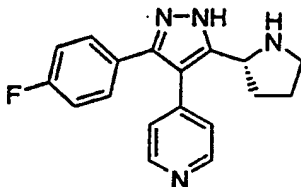
By following the method of Example C-1 and substituting (S)-N-t-butoxycarbonyl-prolinyl N-hydroxysuccinimide for N-benzyloxycarbonyl-glyciny N-hydroxysuccinimide the title compound was prepared as the N-t-butoxycarbonyl protected compound. The deprotection of the N-t-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 309 (base peak).

**Example C-124****(S)-5-(N-METHYL-2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-****FLUOROPHENYL) PYRAZOLE**

By following the method of Example C-75 and substituting (S)-5-(2-pyrrolidiny1)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-123) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 323 (base peak).

**Example C-125**

**(R)-5-(2-PYROLIDINY1)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE**

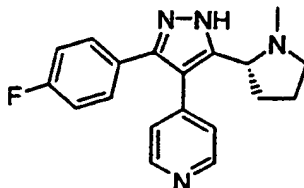


By following the method of Example C-1 and substituting (R)-N-t-butoxycarbonyl-prolinyl N-hydroxysuccinimide for N-benzyloxycarbonyl-glycinyl N-hydroxysuccinimide the title compound was prepared as the N-t-butoxycarbonyl protected compound. The deprotection of the N-t-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 309 (base peak).



## Example C-126

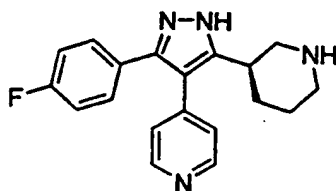
(R)-5-(N-METHYL-2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-  
FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting (R)-5-(2-pyrrolidinyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-125) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 323 (base peak).

## Example C-127

(R)-5-(3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE



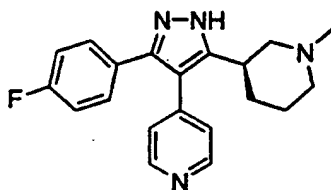
By following the method of Example C-1 and substituting (R)-N-t-butoxycarbonyl-nipecotyl N-hydroxysuccinimide for N-benzyloxycarbonyl-glycyl N-

964

hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 323 (base peak).

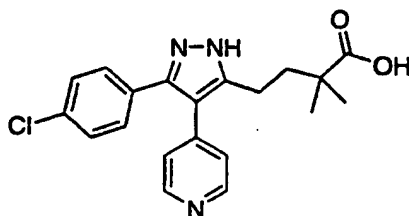
**Example C-128**

**(R)-5-(*N*-METHYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

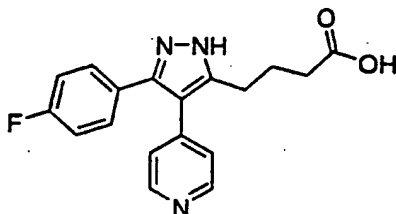


By following the method of Example C-75 and substituting (R)-5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-125) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 337 (base peak).

965

**Example C-129****2,2-DIMETHYL-4-[4-(4-PYRIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLYL] BUTYRIC ACID**

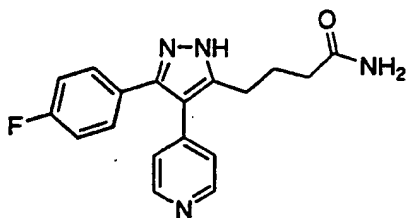
By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and 2,2-dimethyl glutaric anhydride for *N*-benzyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 370 (base peak).

**Example C-130****4-[4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL] BUTYRIC  
ACID**

By following the method of Example C-1 and substituting glutaric anhydride for *N*-benzyloxycarbonyl-glycinyll *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 326 (base peak).

## Example C-131

## 4-[4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL] BUTYRAMIDE

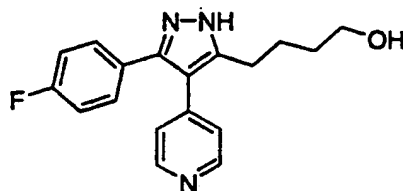


**Methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate.** To a solution of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyric acid (Example C-130) (40 g, 123 mmol) in 650 mL of MeOH was added 20 mL of concentrated H<sub>2</sub>SO<sub>4</sub>. The solution was stirred overnight at room temperature. The solution was concentrated and diluted with 200 mL of water. The solution was cooled with an ice/water bath and to the solution was added 150 mL of saturated NaHCO<sub>3</sub>. The solution was neutralized further with 50% NaOH to pH 7. The resulting slurry was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 250 mL). The combined extracts were washed with water (1 x 300 mL) and saturated NaHCO<sub>3</sub> (1 x 500 mL). The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate: MS (M+H): 340 (base peak).

**4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyramide.** A solution of methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate (39 g, 120 mmol) in 600 mL of MeOH was saturated with NH<sub>3</sub>. The solution was

967

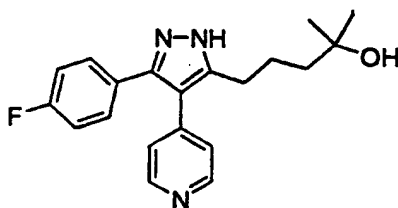
periodically treated with additional  $\text{NH}_3$  over a 24 h period. The solution was degassed with a stream of nitrogen and the solution was concentrated to leave a yellow solid. The solid was slurried in ether and filtered to leave the title compound: MS (M+H): 325 (base peak).

**Example C-132****5-[4-(1-HYDROXY)BUTYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE**

A stirred suspension of 4-(4-(4-pyridyl)-3-(4-fluorophenyl)pyrazolyl) butyric acid (Example C-130) (2 g, 6.15 mmol) in 100 ml of anhydrous ether was cooled to 0 °C under nitrogen. Lithium aluminum hydride (467 mg, 12.3 mmol) was added to this suspension slowly. After the addition was complete, the mixture was warmed to room temperature and stirred for additional 2 h. The reaction was quenched slowly with 1N  $\text{KHSO}_4$  (80 ml). The mixture was transferred to a separatory funnel and the aqueous layer was removed. The aqueous layer was then made basic with  $\text{K}_2\text{CO}_3$  (pH 8). The aqueous solution was extracted with ethyl acetate (2 x 100 mL). The combined ethyl acetate extracts were washed with water (1 x 100

968

mL), dried over  $\text{MgSO}_4$ , filtered and concentrated to give the title compound: MS (M+H): 312 (base peak).

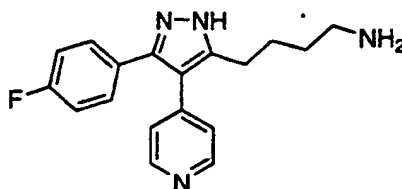
**Example C-133****5-[4-(1,1-DIMETHYL-1-HYDROXY)BUTYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE**

A solution of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyric acid (Example C-130) (200 mg, 0.615 mmol) in 50 ml of MeOH was treated with 10 ml of 4 N HCl/dioxane. The reaction mixture was stirred for 5 hours and evaporated to dryness. To this residue was added 15 ml of 1N methyl magnesium bromide in butyl ether and 5 ml of anhydrous THF. The reaction was heated to reflux under nitrogen for 64 h.

The reaction was quenched with 20 ml of saturated ammonium chloride. This mixture was transferred to a separatory funnel and was extracted with 100 ml ethyl acetate (2 x 100 mL). The combined ethyl acetate extracts were washed with water (1 x 100 mL), dried over  $\text{MgSO}_4$ , filtered and concentrated to afford a crude oil. The crude oil was subjected to column chromatography by using 3.5 % MeOH/ $\text{CH}_2\text{Cl}_2$ , followed by 6 % MeOH/ $\text{CH}_2\text{Cl}_2$ , to give the title compound: MS (M+H): 340 (base peak).

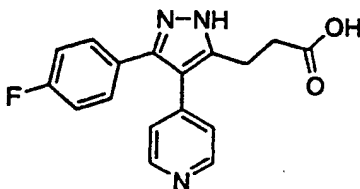
## Example C-134

5-(4-(1-AMINO)BUTYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE

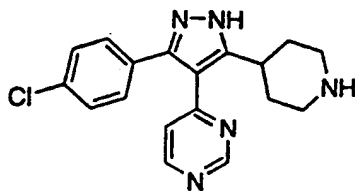


To a suspension of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyramide (Example C-131) (2 g, 6.2 mmol) in 100 ml of anhydrous ether was added lithium aluminum hydride (467 mg, 12.3 mmol). After the addition was complete, the mixture was warmed to room temperature and stirred for additional 2 h. The reaction was quenched with 20 mL of ethyl acetate and was poured onto 100 mL of 2.5 N NaOH. The mixture was extracted with ethyl acetate (3 x 50 mL). The combined extracts were washed with brine (1 x 100 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford the title compound: MS (M+H): 311 (base peak).

970

**Example C-135****4-(4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL) PROPIONIC  
ACID**

By following the method of Example C-1 and substituting succinic anhydride for *N*-benzyloxycarbonyl-glyciny *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 312 (base peak).

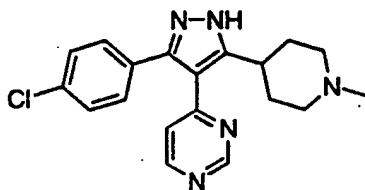
**Example C-136****5-(4-PIPERIDYL)-4-(4-PYRIMIDYL)-3-(4-CHLOROPHENYL)  
PYRAZOLE**

By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate, *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benzyloxycarbonyl-glyciny *N*-hydroxysuccinimide and 4-methylpyrimidine for 4-picoline



971

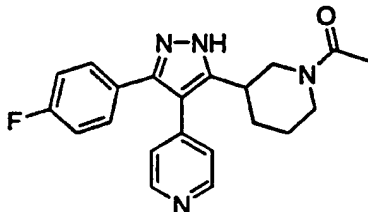
the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.2 (s, 1 H), 8.48 (d,  $J$  = 5.19 Hz, 1 H), 7.31 (m, 4 H), 6.94 (d,  $J$  = 4.79 Hz, 1 H), 3.69 (m, 3 H), 3.12 (m, 2 H), 2.3 (m, 3 H), 1.24 (m, 2 H). MS ( $M+H$ ): 340 (base peak).

**Example C-137****5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIMIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE**

By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-136) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.2 (d,  $J$  = 1.2 Hz, 1 H), 8.48 (d,  $J$  = 5.59 Hz, 1 H), 7.31 (m, 4 H), 6.95 (dd,  $J$  = 1.2, 5.6 Hz, 1 H), 3.39 (m, 1 H), 3.03 (d,  $J$  = 11.6 Hz, 2 H), 2.38 (s, 3 H), 2.06 (m, 4 H), 1.24 (m, 2 H). MS ( $M+H$ ): 354 (base peak).

**Example C-138**

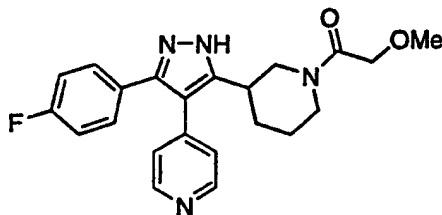
**5-(N-ACETYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL)  
PYRAZOLE**



By following the method of Example C-76 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (C-74) the title compound was prepared: MS (M+H): 365 (base peak).

**Example C-139**

**5-(N-METHOXYACETYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-  
FLUOROPHENYL) PYRAZOLE**



By following the method of Example C-76 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (C-74) and methoxy

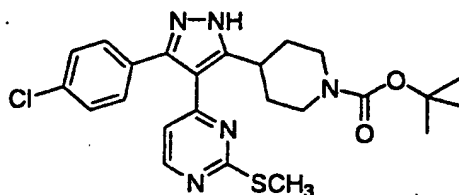
973

acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 395 (base peak).

Additional compounds of the present invention which could be prepared using one or more of the reaction schemes set forth in this application include, but are not limited to, the following:

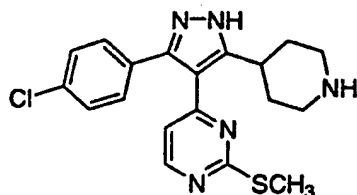
**Example C-140**

**5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**



**Example C-141**

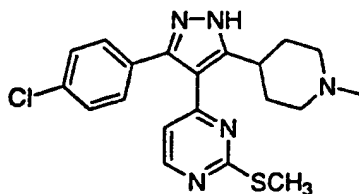
**5-(4-piperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**



974

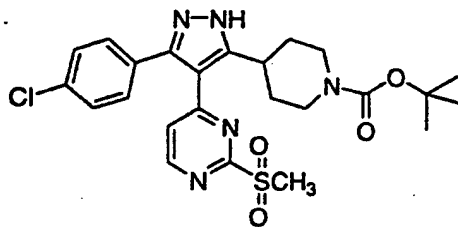
## Example C-142

5-(4-*N*-methylpiperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



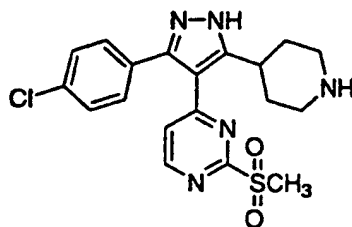
## Example C-143

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



## Example C-144

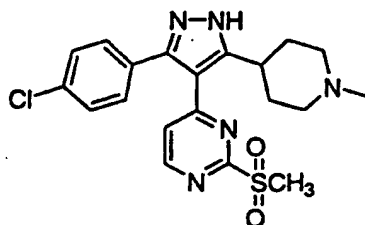
5-(4-piperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



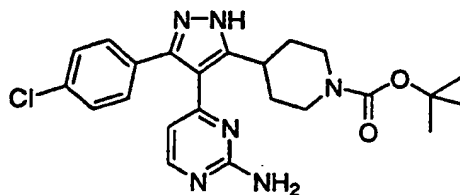
975

**Example C-145**

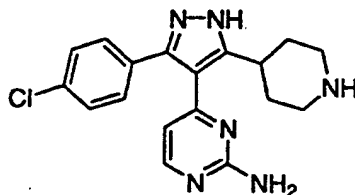
**5-(4-N-methylpiperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

**Example C-146**

**5-(4-N-t-butoxycarbonylpiperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

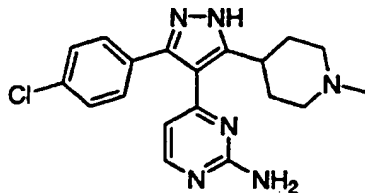
**Example C-147**

**5-(4-piperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

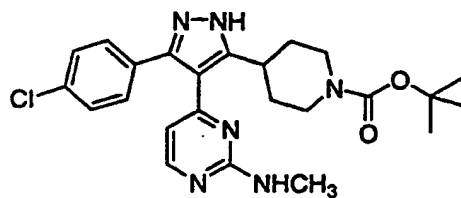


**Example C-148**

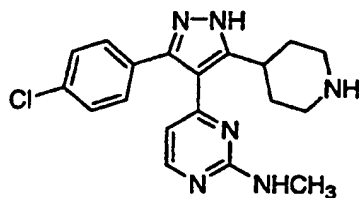
**5-(4-N-methylpiperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

**Example C-149**

**5-(4-N-t-butoxycarbonylpiperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

**Example C-150**

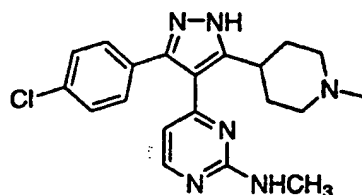
**5-(4-piperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**



977

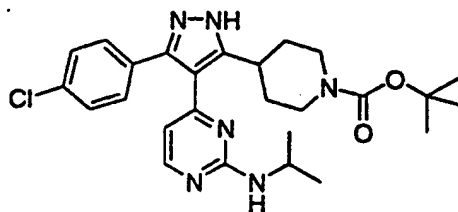
## Example C-151

5-(4-*N*-methylpiperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



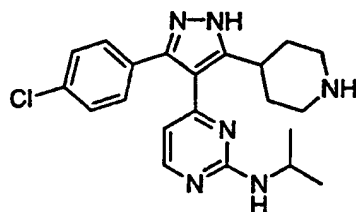
## Example C-152

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



## Example C-153

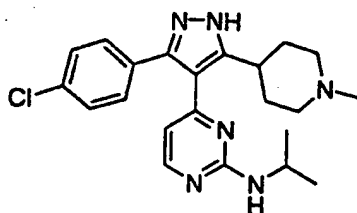
5-(4-piperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



978

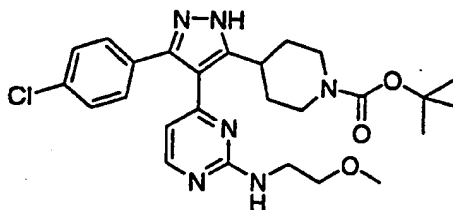
## Example C-154

5-(4-*N*-methylpiperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



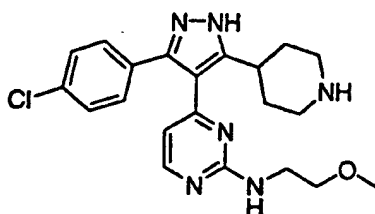
## Example C-155

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole



## Example C-156

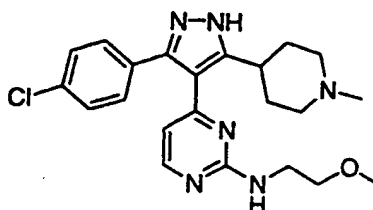
5-(4-piperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole



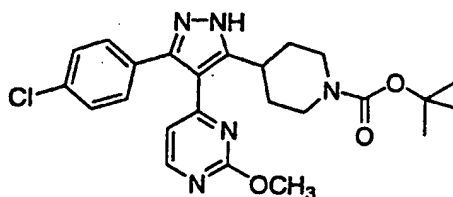


**Example C-157**

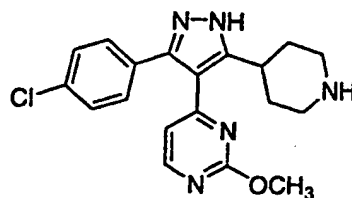
**5-(4-*N*-methylpiperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

**Example C-158**

**5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**

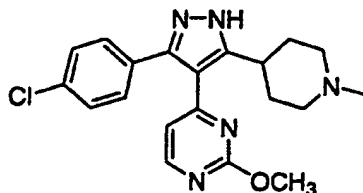
**Example C-159**

**5-(4-piperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole**



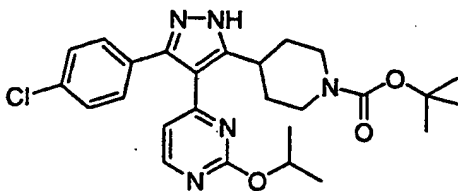
## Example C-160

5-(4-*N*-methylpiperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



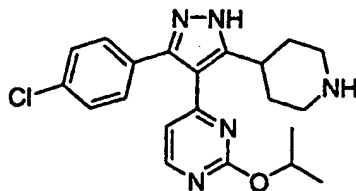
## Example C-161

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



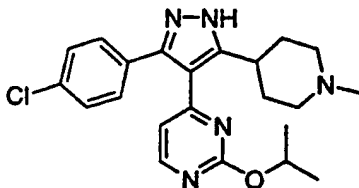
## Example C-162

5-(4-piperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



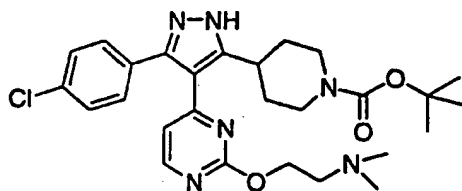
## Example C-163

5-(4-*N*-methylpiperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



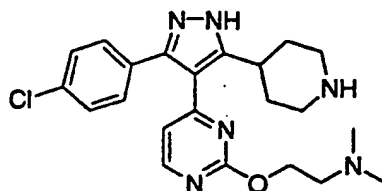
## Example C-164

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-(2-*N,N*-dimethylamino)ethoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



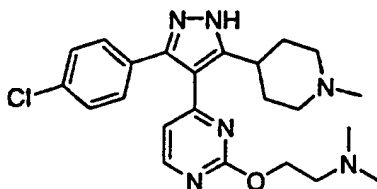
## Example C-165

5-(4-piperidinyl)-4-[4-(2-(2-*N,N*-dimethylamino)ethoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



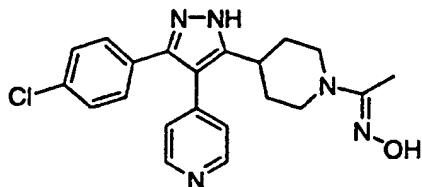
### Example C-166

5-(4-N-methylpiperidiny1)-4-[4-(2-(2-N,N-dimethylamino)ethoxy)pyrimidiny1]-3-(4-chlorophenyl)pyrazole



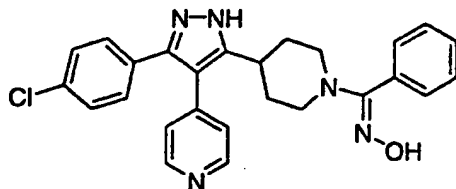
### Example C-167

5-(*N*-acetylhydroxylimido-4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



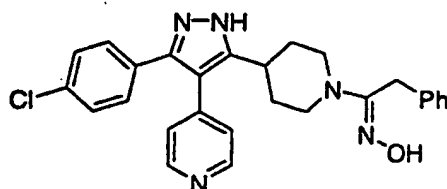
### Example C-168

5-(*N*-benzylhydroxylimido-4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



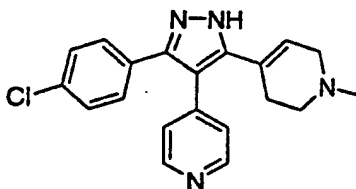
## Example C-169

5-(*N*-phenylacethydroxylimido-4-piperidyl)-4-(4-pyridyl)-  
3-(4-chlorophenyl)pyrazole



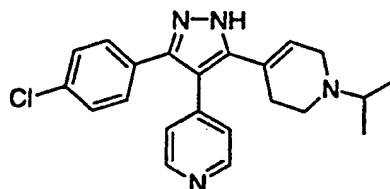
## Example C-170

5-[*N*-methyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-(4-  
chlorophenyl)pyrazole



## Example C-171

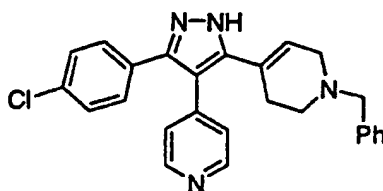
5-[*N*-isopropyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-  
(4-chlorophenyl)pyrazole



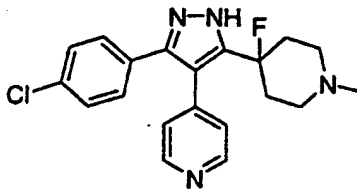
984

**Example C-172**

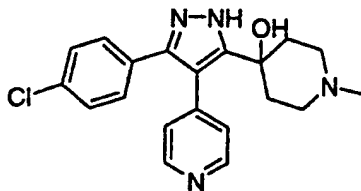
**5-[N-benzyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-173**

**5-[N-methyl-4-(4-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-174**

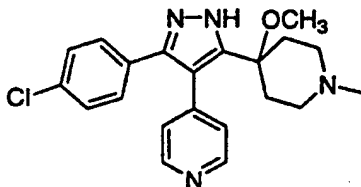
**5-[N-methyl-4-(4-hydroxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



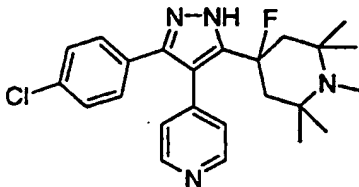
985

**Example C-175**

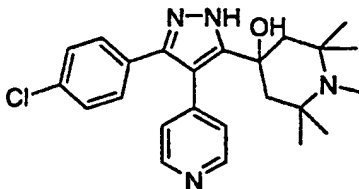
**5-[N-methyl-4-(4-methoxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-176**

**5-[N-methyl-4-(2,5-tetramethyl-4-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-177**

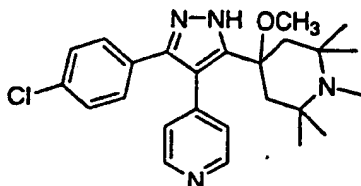
**5-[N-methyl-4-(2,5-tetramethyl-4-hydroxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



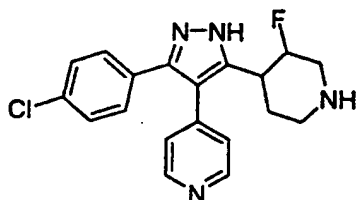
986

**Example C-178**

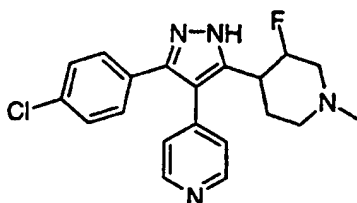
**5-[*N*-methyl-4-(2,5-tetramethyl-4-methoxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-179**

**5-[4-(3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-180**

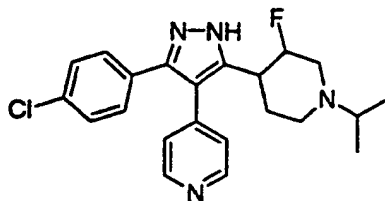
**5-[4-(*N*-methyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



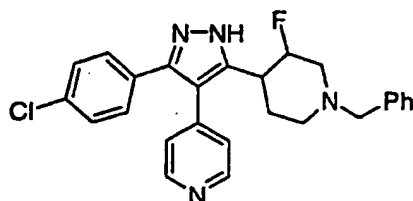


**Example C-181**

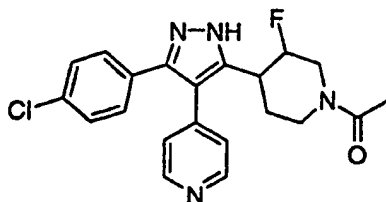
**5-[4-(*N*-isopropyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-182**

**5-[4-(*N*-benzyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

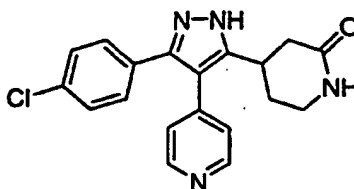
**Example C-183**

**5-[4-(*N*-acetyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

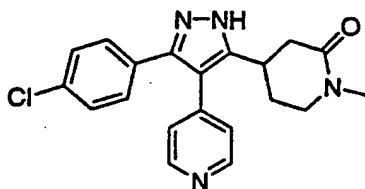


**Example C-184**

**5-[4-(2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-185**

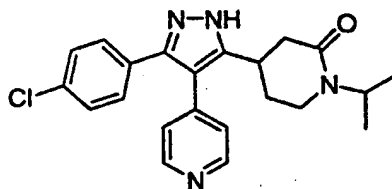
**5-[4-(N-methyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



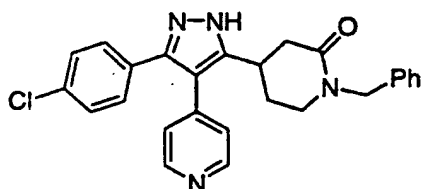
989

**Example C-186**

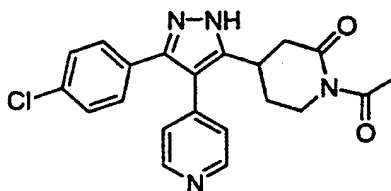
**5-[4-(*N*-isopropyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-187**

**5-[4-(*N*-benzyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-188**

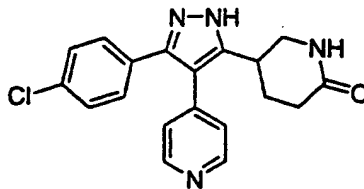
**5-[4-(*N*-acetyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



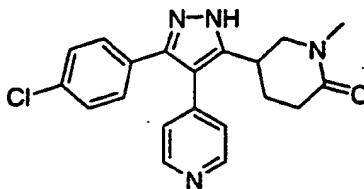
990

**Example C-189**

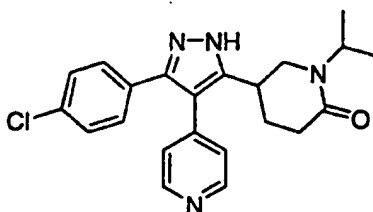
**5-[5-(2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-190**

**5-[5-(N-methyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-191**

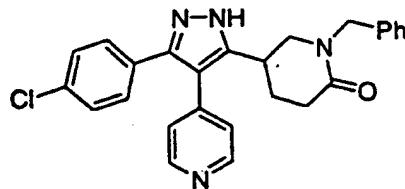
**5-[5-(N-isopropyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



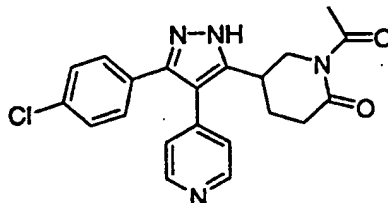
991

**Example C-192**

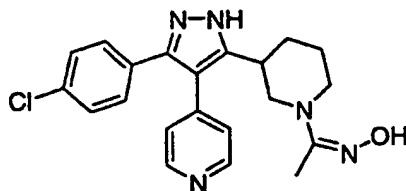
**5-[5-(*N*-benzyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-193**

**5-[5-(*N*-acetyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

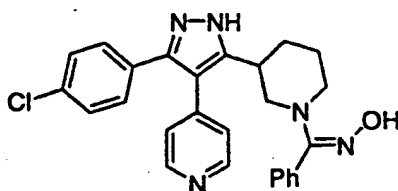
**Example C-194**

**5-(*N*-acethydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

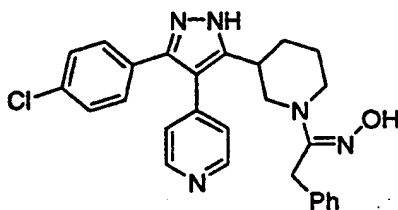


**Example C-195**

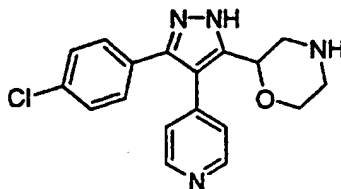
**5-(*N*-benzhydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-196**

**5-(*N*-phenacethydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

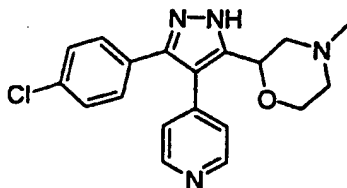
**Example C-197**

**5-(2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

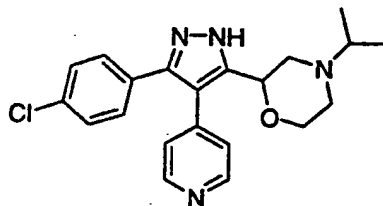


**Example C-198**

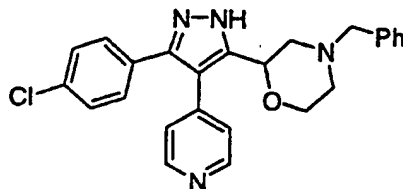
**5-(*N*-methyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-199**

**5-(*N*-isopropyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

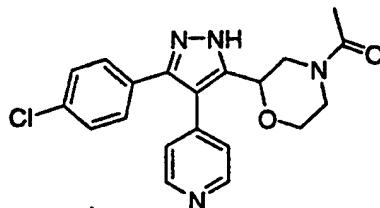
**Example C-200**

**5-(*N*-benzyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

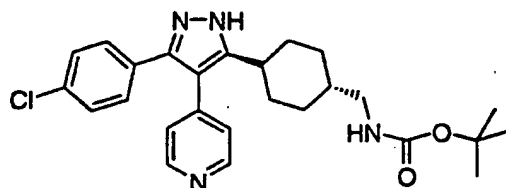


**Example C-201**

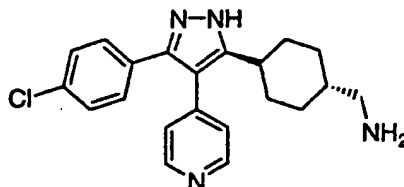
**5-(*N*-acetyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-202**

**5-[*trans*-4-(*N*-*t*-butoxycarbonylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-203**

**5-(*trans*-4-aminomethylcyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

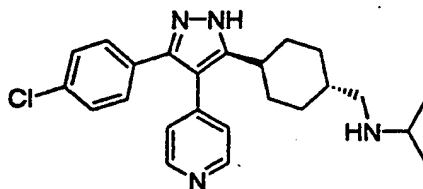




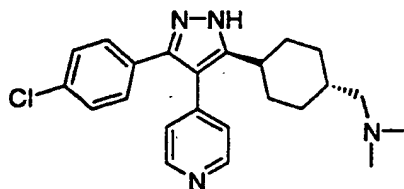
995

**Example C-204**

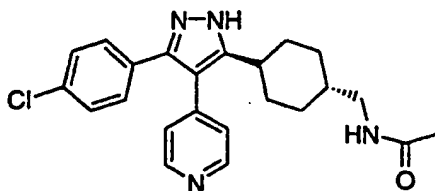
**5-[trans-4-(*N*-isopropylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-205**

**5-[trans-4-(*N,N*-dimethylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

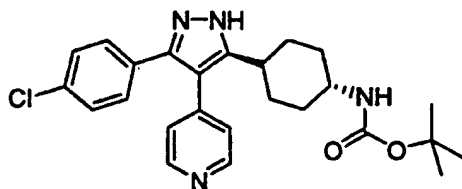
**Example C-206**

**5-[trans-4-(*N*-acetylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

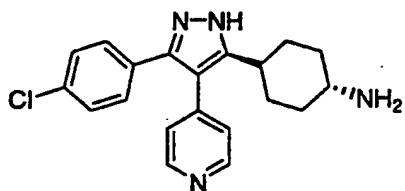


**Example C-207**

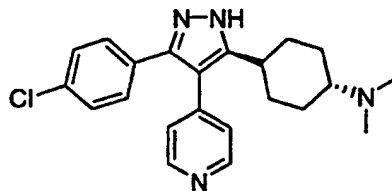
**5-[trans-4-(*N*-*t*-butoxycarbonylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-208**

**5-(trans-4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

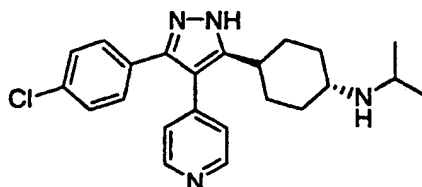
**Example C-209**

**5-[trans-4-(*N,N*-dimethylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

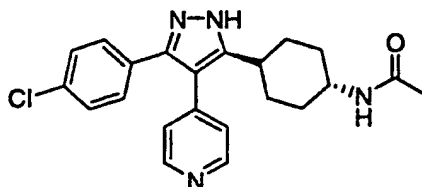


**Example C-210**

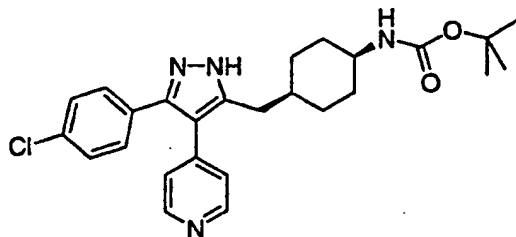
**5-[trans-4-(N-isopropylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-211**

**5-[trans-4-(N-acetylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

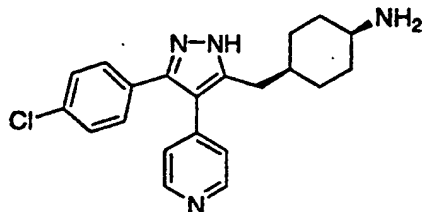
**Example C-212**

**5-[cis-4-(N-t-butoxycarbonyl)methylaminocyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

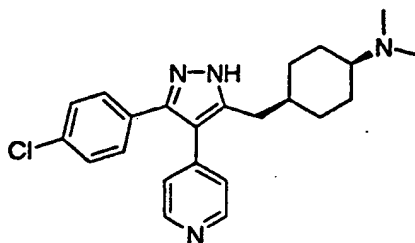


**Example C-213**

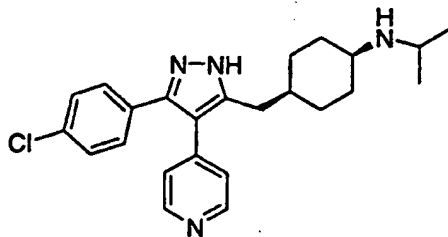
**5-(*cis*-4-methylaminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-214**

**5-[*cis*-4-(*N,N*-dimethyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

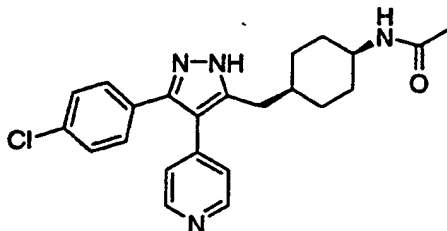
**Example C-215**

**5-[*cis*-4-(*N*-isopropyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

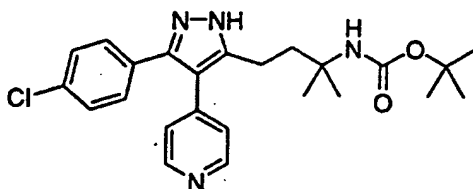


**Example C-216**

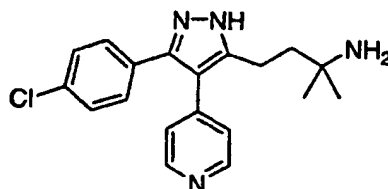
**5-[*cis*-4-(*N*-acetyl)methylaminocyclohexyl]]-4-(4-pyridyl)-  
3-(4-chlorophenyl)pyrazole**

**Example C-217**

**5-[3-(1,1-dimethyl-1-(*N*-*t*-butoxycarbonylamino)propyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-218**

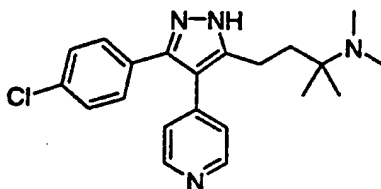
**5-[3-(1,1-dimethyl-1-amino)propyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



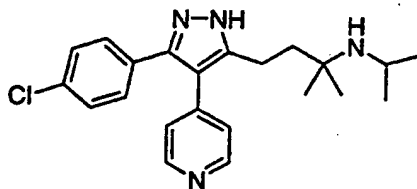
1000

**Example C-219**

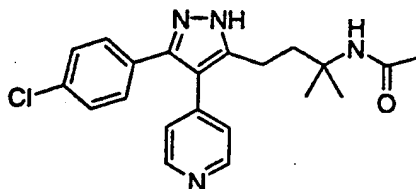
5-[3-(1,1-dimethyl-1-(*N,N*-dimethylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole

**Example C-220**

5-[3-(1,1-dimethyl-1-(*N*-isopropylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole

**Example C-221**

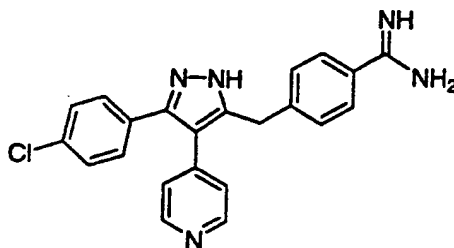
5-[3-(1,1-dimethyl-1-(*N*-acetylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



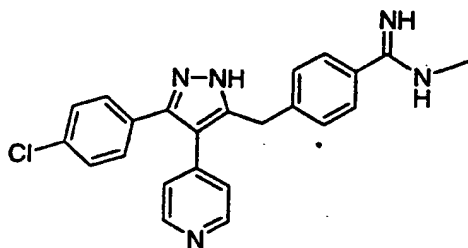
1001

**Example C-222**

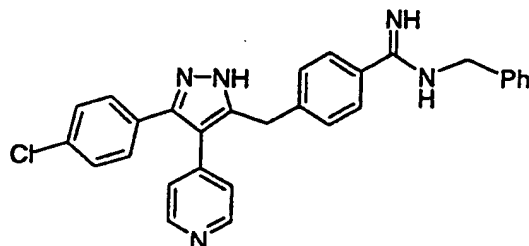
**5-[4-(1-carboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-223**

**5-[4-(1-N-methylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-224**

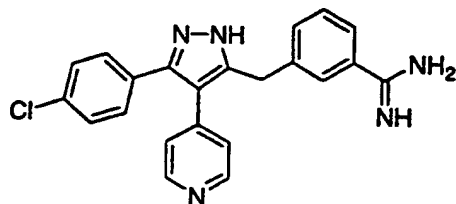
**5-[4-(1-N-benzylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



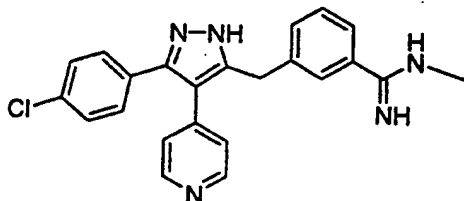
1002

**Example C-225**

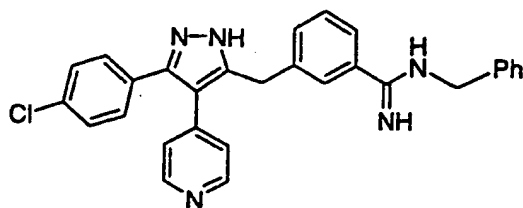
**5-[3-(1-carboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-226**

**5-[3-(1-N-methylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-227**

**5-[3-(1-N-benzylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

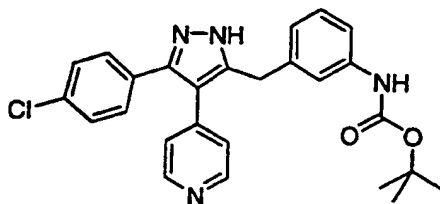




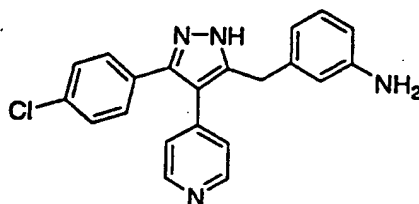
1003

**Example C-228**

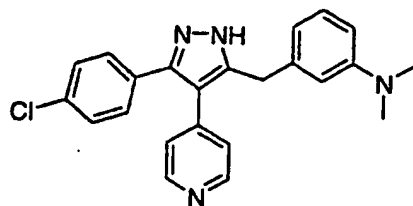
**5-[3-(*N*-*t*-butoxycarbonyl)aminobenzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-229**

**5-(3-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-230**

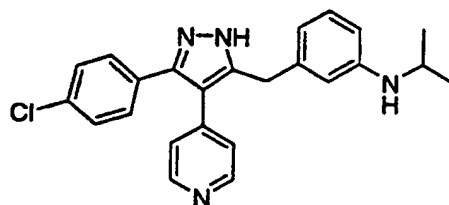
**5-[3-(*N,N*-dimethylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



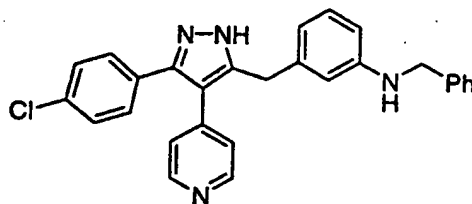
1004

**Example C-231**

**5-[3-(*N*-isopropylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-232**

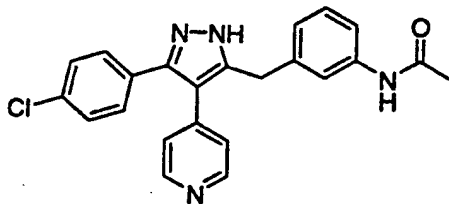
**5-[3-(*N*-benzylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



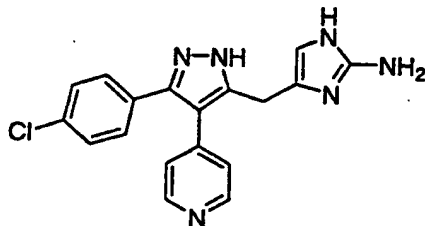
1005

**Example C-233**

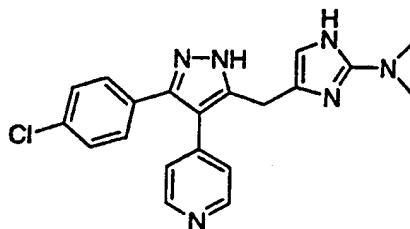
5-[3-(*N*-acetylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole

**Example C-234**

5-[4-(2-amino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole

**Example C-235**

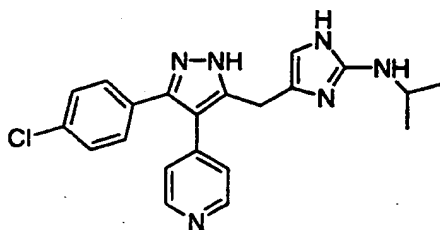
5-[4-(2-*N,N*-dimethylamino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



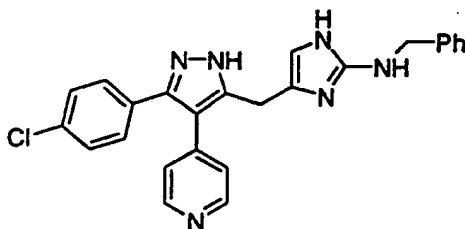
1006

**Example C-236**

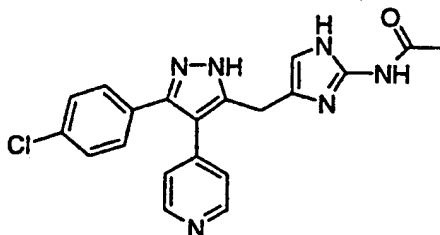
**5-[4-(2-*N*-isopropylamino)methylimidazolyl]-4-(4-pyridyl)-  
3-(4-chlorophenyl)pyrazole**

**Example C-237**

**5-[4-(2-*N*-benzylamino)methylimidazolyl]-4-(4-pyridyl)-3-  
(4-chlorophenyl)pyrazole**

**Example C-238**

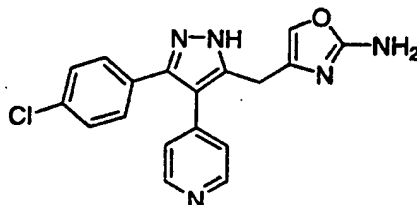
**5-[4-(2-*N*-acetylamino)methylimidazolyl]-4-(4-pyridyl)-3-  
(4-chlorophenyl)pyrazole**



1007

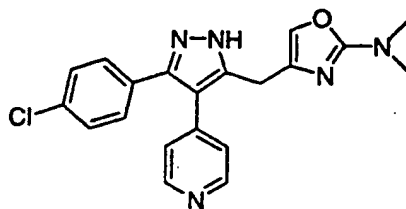
## Example C-239

5-[4-(2-amino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



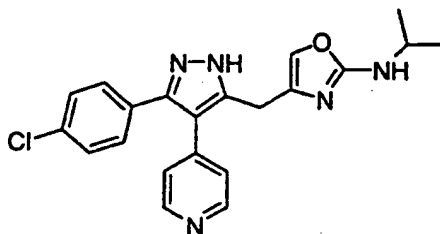
## Example C-240

5-[4-(2-*N,N*-dimethylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



## Example C-241

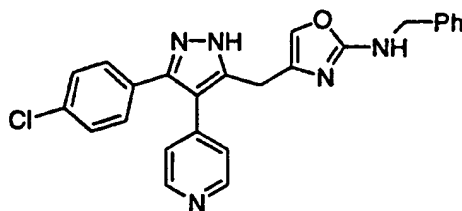
5-[4-(2-*N*-isopropylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



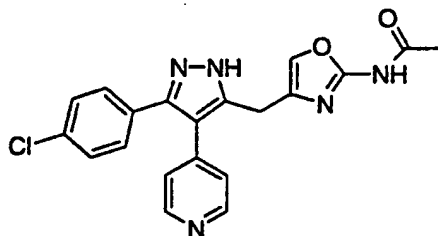
1008

**Example C-242**

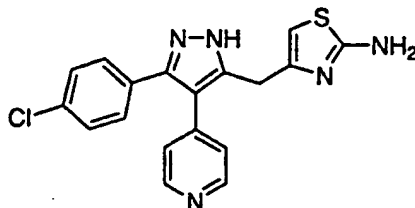
**5-[4-(2-*N*-benzylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-243**

**5-[4-(2-*N*-acetylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-244**

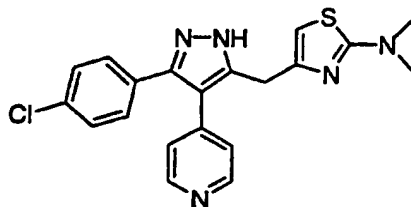
**5-[4-(2-amino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**



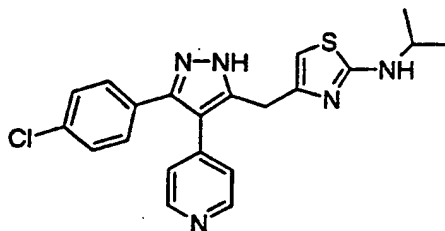
1009

**Example C-245**

**5-[4-(2-*N,N*-dimethylamino)methylthiazolyl]-4-(4-pyridyl)-  
3-(4-chlorophenyl)pyrazole**

**Example C-246**

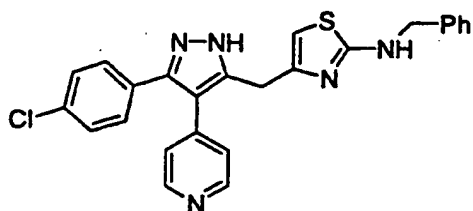
**5-[4-(2-*N*-isopropylamino)methylthiazolyl]-4-(4-pyridyl)-  
3-(4-chlorophenyl)pyrazole**



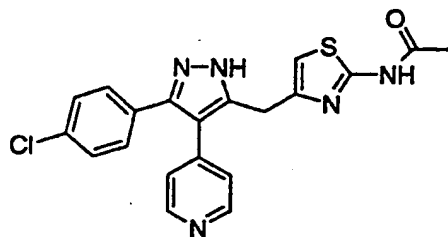
1010

**Example C-247**

**5-[4-(2-*N*-benzylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**

**Example C-248**

**5-[4-(2-*N*-acetylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole**





1011

Biological data from compounds of Examples B-0001 through B-1573 and of Examples B-2270 through B-2462 are shown in the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

**"P38 alpha kinase IC<sub>50</sub>, uM or % inhib @ conc. (uM)"**

10

In vitro whole cell assay for measuring the ability of the compounds to inhibit TNF production in human U937 cells stimulated with LPS are shown in the column identified as:

**"U937 Cell IC<sub>50</sub>, uM or % inhib @ conc., (uM)"**

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the mouse is shown in the column identified as:

**"Mouse LPS Model, % TNF inhib @ dose @ predose time"**

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when the compound is administered.

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

**"Rat LPS Model, % TNF inhib @ dose @ predose time"**

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time

1012

indicates the number of hours before LPS challenge when the compound is administered.

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0001	53.0%@1.0uM	40.0% @1.0uM		
B-0002	71.0%@1.0uM	28.0%@10.0uM		
B-0003	70.0%@1.0uM	76.0% 10.0uM		
B-0004	80.0%@1.0uM	4.61uM		
B-0005	95.0%@1.0uM	2.97uM		
B-0006	82.0%@1.0uM	80.0% @10.0uM		
B-0007	74.0%@1.0uM	85.0% @10.0uM		
B-0008	42.0%@1.0uM	65.0% @10.0uM		
B-0009	0.04 uM	0.72uM		
B-0010	0.52 uM	0.65uM		
B-0011	0.03 uM	4.47uM		
B-0012	30.0%@1.0uM	44.0% @1.0uM		
B-0013	70.0%@1.0uM	84.0% @10.0uM		
B-0014	79.0%@1.0uM	80.0% @10.0uM		
B-0015	82.0%@1.0uM	80.0% @10.0uM		
B-0016	94.0%@1.0uM	3.98uM		
B-0017	56.0%@1.0uM	79.0% @10.0uM		
B-0018	60.0%@1.0uM	59.0% @10.0uM		
B-0019	84.0%@1.0uM	100.0% @10.0uM		
B-0020	73.0%@1.0uM	81.0% @10.0uM		
B-0021	68.0%@1.0uM	76.0% @10.0uM		
B-0022	69.0%@1.0uM	44.0 @1.0uM		
B-0023	90.0%@1.0uM	77.0% @10.0uM		
B-0024	94.0%@1.0uM	52.0% @1.0uM		
B-0025	89.0%@1.0uM	79.0% @10.0uM		
B-0026	96.0%@1.0uM	3.27uM		
B-0027	94.0%@1.0uM	11.0uM		
B-0028	69.0%@1.0uM	45.0% @10.0uM		
B-0029	91.0%@1.0uM	58.0% @10.0uM		
B-0030	92.0%@1.0uM	75.0% @10.0uM		
B-0031	94.0%@1.0uM	100.0% @10.0uM		
B-0032	94.0%@1.0uM	78.0% @10.0uM		
B-0033	97.0%@1.0uM	10.0uM		
B-0034	95.0%@1.0uM	10.0uM		
B-0035	94.0%@1.0uM	10.0uM		
B-0036	92.0%@1.0uM	8.24uM		
B-0037	91.0%@1.0uM	86.0% @10.0uM		
B-0038	71.0%@1.0uM	84.0% @10.0uM		
B-0039	89.0%@1.0uM	72.0% @10.0uM		
B-0040	93.0%@1.0uM	2.3uM		
B-0041	65.0%@1.0uM	66.0% @10.0uM		
B-0042	94.0%@1.0uM	2.76uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0043	0.22 uM	0.54uM		
B-0044	0.14 uM	0.19uM		
B-0045	94.0%@1.0uM	1.01uM		
B-0046	96.0%@1.0uM	54.0%@1.0uM		
B-0047	94.0%@1.0uM	74.0%@10.0uM		
B-0048	94.0%@1.0uM	76.0%@10.0uM		
B-0049	88%@1.0uM	33.0%@1.0uM		
B-0050	73%@1.0uM	34.0%@1.0uM		
B-0051	3.3uM	2.15uM	47%@100mpk@-6h	79%@3mpk@-4h
B-0052	92%@1.0uM	15.0%@1.0uM		
B-0053	95%@1.0uM	34.0%@1.0uM		
B-0054	90%@1.0uM	30.0%@1.0uM		
B-0055	93%@1.0uM	>1.0uM		
B-0056	96%@1.0uM	21.0%@1.0uM		
B-0057	96%@1.0uM	29.0%@1.0uM		
B-0058	79%@1.0uM	18.0%@1.0uM		
B-0059	83%@1.0uM	35.0%@1.0uM		
B-0060	73%@1.0uM	22.0%@1.0uM		
B-0061	62%@1.0uM	27.0%@1.0uM		
B-0062	94%@1.0uM	36.0%@1.0uM		
B-0063	96%@1.0uM	40.0%@1.0uM		
B-0064	90%@1.0uM	4.0%@1.0uM		
B-0065	83%@1.0uM	21.0%@1.0uM		
B-0066	94%@1.0uM	28.0%@1.0uM		
B-0067	91%@1.0uM	1.0%@1.0uM		
B-0068	72%@1.0uM	22.0%@1.0uM		
B-0069	96%@1.0uM	37.0%@1.0uM		
B-0070	92%@1.0uM	30.0%@1.0uM		
B-0071	86%@1.0uM	31.0%@1.0uM		
B-0072	77%@1.0uM	32.0%@1.0uM		
B-0073	91%@1.0uM	24.0%@1.0uM		
B-0074	92%@1.0uM	42.0%@1.0uM		
B-0075	91%@1.0uM	35.0%@1.0uM		
B-0076	58%@1.0uM	21.0%@1.0uM		
B-0077	0.8uM	10.0uM		
B-0078	80%@1.0uM	20.0%@1.0uM		
B-0079	93%@1.0uM	13.0%@1.0uM		
B-0080	73%@1.0uM	73.0%@1.0uM		
B-0081	92%@1.0uM	13.0%@1.0uM		
B-0082	47%@1.0uM	27.0%@1.0uM		
B-0083	0.22uM	6.51uM		
B-0084	56%@1.0uM	30.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0085	83%@1.0uM	21.0%@1.0uM		
B-0086	91%@1.0uM	37.0%@1.0uM		
B-0087	0.55uM	2.26uM	38%@30mpk@-6h	
B-0088	96%@1.0uM	9.0%@1.0uM		
B-0089	0.04uM	3.33uM		
B-0090	98%@1.0uM	52.0%@1.0uM		
B-0091	96%@1.0uM	40.0%@1.0uM		
B-0092	97%@1.0uM	34.0%@1.0uM		
B-0093	3.18 uM	1.25uM	30%@30mpk@-6h	
B-0094	96%@1.0uM	52.0%@1.0uM		
B-0095	98%@1.0uM	38.0%@1.0uM		
B-0096	91%@1.0uM	22.0%@1.0uM		
B-0097	72.0%@10.0uM	38.0%@1.0uM		
B-0098	66.0%@10.0uM	12.0%@1.0uM		
B-0099	43.0% @1.0uM	>1.0uM		
B-0100	75.0% @1.0uM	5.0uM		
B-0101	71.0% @1.0uM	2.11uM		
B-0102	81.0%@1.0uM	15.0%@1.0uM		
B-0103	71.0%@1.0uM	6.0%@1.0uM		
B-0104	56.0% @1.0uM	2.78uM		
B-0105	78.0%@1.0uM	5.0uM		
B-0106	62.0%@1.0uM	5.0uM		
B-0107	0.27uM	5.0uM		
B-0108	61.0%@1.0uM	4.85uM		
B-0109	45.0%@1.0uM	19.0%@1.0uM		
B-0110	66.0%@1.0uM	13.0%@1.0uM		
B-0111	57.0%@1.0uM	>1.0uM		
B-0112	97.0%@1.0uM	1.12uM		
B-0113	75.0%@1.0uM	43.0%@1.0uM		
B-0114	45.0%@1.0uM	3.92uM		
B-0115	47.0%@1.0uM	2.0%@1.0uM		
B-0116	73.0%@1.0uM	35.0%@1.0uM		
B-0117	0.46 uM	1.78 uM	30%@30mpk@-6h	
B-0118	1.18 uM	1.29 uM		
B-0119	89.0%@10.0uM	2.78uM		
B-0120	0.008 uM	0.21 uM	77%@100mpk@-6h	70%@3mpk@-4h
B-0121	79.0%@1.0uM	1.22uM		
B-0122	79.0%@10.0uM	2.0%@1.0uM		
B-0123	59.0%@1.0uM	>1.0uM		
B-0124	73.0%@1.0uM	15.0%@1.0uM		
B-0125	70.0%@10.0uM	17.0%@1.0uM		
B-0126	66.0%@1.0uM	1.57uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0127	82.0%@1.0uM	0.96uM		
B-0128	78.0%@1.0uM	1.81uM		
B-0129	51.0%@1.0uM	31.0%@1.0uM		
B-0130	69.0%@1.0uM	58.0%@1.0uM		
B-0131	43.0%@1.0uM	46.0%@1.0uM		
B-0132	76.0%@1.0uM	8.0%@1.0uM		
B-0133	51.0%@1.0uM	42.0%@1.0uM		
B-0134	60.0%@1.0uM	2.17uM		
B-0135	78.0%@1.0uM	58.0%@1.0uM		
B-0136	77.0%@1.0uM	44.0%@1.0uM		
B-0137	41.0%@1.0uM	37.0%@1.0uM		
B-0138	50.0%@1.0uM	32.0%@1.0uM		
B-0139	54.0%@10.0uM	17.0%@1.0uM		
B-0140	67% @10.0uM	9.0% @1.0uM		
B-0141	78.0% @1.0uM	10.0% @1.0uM		
B-0142	86.0% @1.0uM	12.0% @1.0uM		
B-0143	42.0% @1.0uM	3.63uM		
B-0144	86.0% @1.0uM	43.0% @1.0uM		
B-0145	54.0% @10.0uM	12.0% @1.0uM		
B-0146	77.0% @10.0uM	28.0% @1.0uM		
B-0147	44.0% @1.0uM	22.0% @1.0uM		
B-0148	51.0% @1.0uM	>1.0uM		
B-0149	1.15 uM	10.0 uM		
B-0150	27.0% @10.0uM	35.0% @1.0uM		
B-0151	43.0% @1.0uM	30.0% @1.0uM		
B-0152	51.0% @1.0uM	24.0% @1.0uM		
B-0153	57.0% @1.0uM	21.0% @1.0uM		
B-0154	65.0% @10.0uM	14.0% @1.0uM		
B-0155	40.0% @10.0uM	26.0% @1.0uM		
B-0156	42.0% @10.0uM	13.0% @1.0uM		
B-0157	48.0% @10.0uM	9.0% @1.0uM		
B-0158	58.0% @10.0uM	39.0% @1.0uM		
B-0159	54.0% @10.0uM	5.0% @1.0uM		
B-0160	59.0% @10.0uM	26.0% @1.0uM		
B-0161	72.0% @10.0uM	13.0% @1.0uM		
B-0162	23% @1.0uM	2.05 uM		
B-0163	20.0% @10.0uM	10.0% @1.0uM		
B-0164	37.0% @10.0uM	20.0% @1.0uM		
B-0165	70.0% @10.0uM	19.0% @1.0uM		
B-0166	45.0% @10.0uM	37.0% @1.0uM		
B-0167	40.0% @1.0uM	37.0% @1.0uM		
B-0168	44% @1.0uM	2.36 uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0169	43.0% @1.0uM	21.0% @1.0uM		
B-0170	43.0% @1.0uM	30.0% @1.0uM		
B-0171	61.0% @10.0uM	21.0% @1.0uM		
B-0172	16.0% @10.0uM	11.0% @1.0uM		
B-0173	33.0% @10.0uM	48.0% @1.0uM		
B-0174	54.0% @10.0uM	43.0% @1.0uM		
B-0175	41.0% @10.0uM	31.0% @1.0uM		
B-0176	50.0% @1.0uM	30.0% @1.0uM		
B-0177	70.0% @10.0uM	27.0% @1.0uM		
B-0178	12.0% @10.0uM	35.0% @1.0uM		
B-0179	27.0% @10.0uM	37.0% @1.0uM		
B-0180	34.0% @10.0uM	23.0% @1.0uM		
B-0181	5.0% @1.0uM	2.0% @1.0uM		
B-0182	39.0% @10.0uM	40.0% @1.0uM		
B-0183	12.0% @10.0uM	34.0% @1.0uM		
B-0184	66.0% @10.0uM	17.0% @1.0uM		
B-0185	65.0% @10.0uM	25.0% @1.0uM		
B-0186	40.0% @1.0uM	25.0% @1.0uM		
B-0187	4.0% @10.0uM	14.0% @1.0uM		
B-0188	70.0% @10.0uM	35.0% @1.0uM		
B-0189	42.0% @10.0uM	9.0% @1.0uM		
B-0190	59.0% @10.0uM	31.0% @1.0uM		
B-0191	40.0% @1.0uM	29.0% @1.0uM		
B-0192	12.0% @10.0uM	47.0% @1.0uM		
B-0193	0.54 uM	6% @1.0uM		
B-0194	1.31 uM	22% @1.0uM		
B-0195	1.03 uM	55% @1.0uM		
B-0196	2.24 uM	>1.0uM		
B-0197	2.0 uM	14% @1.0uM		
B-0198	1.2 uM	2% @1.0uM		
B-0199	1.34 uM	3% @1.0uM		
B-0200	1.31 uM	16% @1.0uM		
B-0201	0.29 uM	59% @1.0uM		
B-0202	0.55 uM	2.26 uM		
B-0203	0.16 uM	65% @1.0uM		
B-0204	0.21 uM	48% @1.0uM		
B-0205	0.096 uM	54% @1.0uM		
B-0206	5.76 uM	14% @1.0uM		
B-0207	0.12 uM	52% @1.0uM		
B-0208	0.067 uM	>1.0uM		
B-0209	0.29 uM	8% @1.0uM		
B-0210	0.057 uM	67% @1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0211	0.25 uM	30%@1.0uM		
B-0212	0.12 uM	28%@1.0uM		
B-0213	0.31 uM	39%@1.0uM		
B-0214	0.16 uM	50%@1.0uM		
B-0215	0.11 uM	51%@1.0uM		
B-0216	0.56 uM	>1.0uM		
B-0217	0.55 uM	>1.0uM		
B-0218	0.53 uM	18%@1.0uM		
B-0219	0.91 uM	18%@1.0uM		
B-0220	0.13 uM	40%@1.0uM		
B-0221	2.4 uM	>1.0uM		
B-0222	0.4uM	29.0%@1.0uM		
B-0223	0.2uM	1.0%@1.0uM		
B-0224	<0.1uM	93.0%@1.0uM		
B-0225	0.047uM	37.0%@1.0uM		
B-0226	0.074uM	20.0%@1.0uM		
B-0227	0.045uM	1.0%@1.0uM		
B-0228	0.15uM	44.0%@1.0uM		
B-0229	<0.1uM	61.0%@1.0uM		
B-0230	0.041uM	30.0%@1.0uM		
B-0231	0.055uM	40.0%1.0uM		
B-0232	0.048uM	24.0%@1.0uM		
B-0233	0.095uM	43.0%@1.0uM		
B-0234	0.11uM	68.0%@1.0uM		
B-0235	1.31uM	90.0%@1.0uM		
B-0236	0.077uM	46.0%@1.0uM		
B-0237	0.13uM	60.0%@1.0uM		
B-0238	0.47uM	82.0%@1.0uM		
B-0239	5.73uM	84.0%@1.0uM		
B-0240	0.2uM	70.0%@1.0uM		
B-0241	0.1uM	45.0%@1.0uM		
B-0242	<0.1uM	78.0%@1.0uM		
B-0243	0.039uM	53.0%@1.0uM		
B-0244	0.02uM	57.0%@1.0uM		
B-0245	0.13uM	24.0%@1.0uM		
B-0246	<0.1uM	>1.0uM		
B-0247	0.082uM	75.0%@1.0uM		
B-0248	<0.1uM	11.0%@1.0uM		
B-0249	<0.1uM	75.0%@1.0uM		
B-0250	0.28uM	36.0%@1.0uM		
B-0251	0.31uM	1.0%@1.0uM		
B-0252	0.041uM	54.0%@1.0uM		



Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0253	0.061uM	74.0%@1.0uM		
B-0254	0.12uM	59.0%@1.0uM		
B-0255	0.32uM	68.0%@1.0uM		
B-0256	<0.1uM	88.0%@1.0uM		
B-0257	1.71uM	11.0%@1.0uM		
B-0258	0.37uM	63.0%@1.0uM		
B-0259	0.35uM	58.0%@1.0uM		
B-0260	0.56uM	23.0%@1.0uM		
B-0261	0.49uM	23.0%@1.0uM		
B-0262	0.41uM	89.0%@1.0uM		
B-0263	0.62uM	64.0%@1.0uM		
B-0264	0.14uM	18.0%@1.0uM		
B-0265	0.92uM	24.0%@1.0uM		
B-0266	0.25uM	24.0%@1.0uM		
B-0267	0.48uM	11.0%@1.0uM		
B-0268	3.39uM	19.0%@1.0uM		
B-0269	9.81uM	19.0%@1.0uM		
B-0270	5.79uM	13.0%@1.0uM		
B-0271	7.55uM	12.0%@1.0uM		
B-0272	1.81uM	48.0%@1.0uM		
B-0273	5.03uM	13.0%@1.0uM		
B-0274	2.68uM	25.0%@1.0uM		
B-0275	2.67uM	33.0%@1.0uM		
B-0276	1.25uM	26.0%@1.0uM		
B-0277	0.68uM	34.0%@1.0uM		
B-0278	1.26uM	36.0%@1.0uM		
B-0279	1.39uM	33.0%@1.0uM		
B-0280	0.86uM	18.0%@1.0uM		
B-0281	7.37uM	24.0%@1.0uM		
B-0282	0.75uM	38.0%@1.0uM		
B-0283	6.66uM	29.0%@1.0uM		
B-0284	0.083uM	65.0%@1.0uM		
B-0285	4.57uM	29.0%@1.0uM		
B-0286	0.33uM	50.0%@1.0uM		
B-0287	4.0uM	22.0%@1.0uM		
B-0288	4.46uM	26.0%@1.0uM		
B-0289	0.15uM	55.0%@1.0uM		
B-0290	0.66uM	44.0%@1.0uM		
B-0291	1.33uM	20.0%@1.0uM		
B-0292	0.22uM	28.0%@1.0uM		
B-0293	0.66uM	53.0%@1.0uM		
B-0294	0.68uM	45.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0295	0.82uM	45.0%@1.0uM		
B-0296	8.03uM	36.0%@1.0uM		
B-0297	0.78uM	30.0%@1.0uM		
B-0298	0.58uM	48.0%@1.0uM		
B-0299	0.87uM	54.0%@1.0uM		
B-0300	0.78uM	32.0%@1.0uM		
B-0301	0.19uM	50.0%@1.0uM		
B-0302	4.02uM	24.0%@1.0uM		
B-0303	0.22uM	10.0%@1.0uM		
B-0304	0.56uM	28.0%@1.0uM		
B-0305				
B-0306				
B-0307				
B-0308				
B-0309				
B-0310				
B-0311				
B-0312				
B-0313				
B-0314				
B-0315				
B-0316				
B-0317				
B-0318				
B-0319				
B-0320				
B-0321				
B-0322				
B-0323				
B-0324				
B-0325				
B-0326				
B-0327				
B-0328				
B-0329				
B-0330				
B-0331				
B-0332				
B-0333				
B-0334				
B-0335				
B-0336				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0337				
B-0338				
B-0339				
B-0340				
B-0341				
B-0342				
B-0343				
B-0344				
B-0345				
B-0346				
B-0347				
B-0348				
B-0349				
B-0350				
B-0351				
B-0352				
B-0353	1.37uM	55%@1.0uM		
B-0354	1.0uM	0.66uM	51%@30mpk@-6h	54%@3mpk@-4h
B-0355	0.75uM	40.0%@1.0uM		
B-0356	0.66uM	24.0%@1.0uM		
B-0357	1.46uM	0.66uM		
B-0358	0.37uM	17.0%@1.0uM		
B-0359	0.45uM	47.0%@1.0uM		
B-0360	1.6uM	19.0%@1.0uM		
B-0361	0.33uM	46.0%@1.0uM		
B-0362	0.52uM	27.0%@1.0uM		
B-0363	4.67uM	25.0%@1.0uM		
B-0364	1.44uM	27.0%@1.0uM		
B-0365	0.96uM	27.0%@1.0uM		
B-0366	0.7uM	46.0%@1.0uM		
B-0367	1.0uM	23.0%@1.0uM		
B-0368	1.0uM	0.64uM	37%@30mpk@-6h	
B-0369	0.16uM	57.0%@1.0uM		
B-0370	0.65uM	28.0%@1.0uM		
B-0371	0.49uM	28.0%@1.0uM		
B-0372	0.35uM	29.0%@1.0uM		
B-0373	0.45uM	18.0%@1.0uM		
B-0374	1.38uM	12.0%@1.0uM		
B-0375	1.0uM	19.0%@1.0uM		
B-0376	2.99uM	12.0%@1.0uM		
B-0377	1.29uM	36.0%@1.0uM		
B-0378	1.1uM	36.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0379	0.53uM	24.0%@1.0uM		
B-0380	1.41uM	32.0%@1.0uM		
B-0381	0.22uM	47.0%@1.0uM		
B-0382	0.41uM	32.0%@1.0uM		
B-0383	1.43uM	10.0%@1.0uM		
B-0384	4.02uM	16.0%@1.0uM		
B-0385	0.057uM	0.9uM	30%@30mpk@-6h	0%@3mpk@-4h
B-0386	0.13uM	54.0%@1.0uM		
B-0387	0.41uM	52.0%@1.0uM		
B-0388	<0.1uM	36.0%@1.0uM		
B-0389	0.01uM	0.05uM		62%@3mpk@-4h
B-0390	0.089uM	55.0%@1.0uM		
B-0391	0.86uM	18.0%@1.0uM		
B-0392	0.13uM	57.0%@1.0uM		
B-0393	0.043uM	66.0%@1.0uM		
B-0394	0.13uM	45.0%@1.0uM		
B-0395	0.087uM	48.0%@1.0uM		
B-0396	0.097uM	0.44uM		
B-0397	0.17uM	41.0%@1.0uM		
B-0398	0.054uM	66.0%@1.0uM		
B-0399	0.14uM	39.0%@1.0uM		
B-0400	0.16uM	25.0%@1.0uM		
B-0401	0.46uM	52.0%@1.0uM		
B-0402	0.14uM	1.51uM		
B-0403	1.77uM	2.42uM		
B-0404	0.31uM	48.0%@1.0uM		
B-0405	0.79uM	30.0%@1.0uM		
B-0406	0.54uM	35.0%@1.0uM		
B-0407	0.76uM	27.0%@1.0uM		
B-0408	0.5uM	50.0%@1.0uM		
B-0409	0.53uM	30.0%@1.0uM		
B-0410	0.38uM	44.0%@1.0uM		
B-0411	0.62uM	50.0%@1.0uM		
B-0412	0.24uM	48.0%@1.0uM		
B-0413	0.18uM	55.0%@1.0uM		
B-0414	2.54uM	25.0%@1.0uM		
B-0415	0.42uM	43.0%@1.0uM		
B-0416	0.32uM	34.0%@1.0uM		
B-0417	0.91uM	28.0%@1.0uM		
B-0418	0.22uM	27.0%@1.0uM		
B-0419	0.85uM	41.0%21.0uM		
B-0420	0.83uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0421	0.46uM	57.0%@1.0uM		
B-0422	<0.1uM	40.0%@1.0uM		
B-0423	0.18uM	33.0%@1.0uM		
B-0424	0.083uM	32.0%@1.0uM		
B-0425	0.26uM	54.0%@1.0uM		
B-0426	0.055uM	0.74uM		41%@3mpk@-4h
B-0427	0.63uM	39.0%@1.0uM		
B-0428	0.99uM	27.0%@1.0uM		
B-0429	0.27uM	45.0%@1.0uM		
B-0430	0.29uM	75.0%@1.0uM		
B-0431	0.21uM	64.0%@1.0uM		
B-0432	<0.1uM	89.0%@1.0uM		
B-0433	<0.1uM	92.0%@1.0uM		
B-0434	0.12uM	65.0%@1.0uM		
B-0435	0.3uM	61.0%@1.0uM		
B-0436	1.11uM	71.0%@1.0uM		
B-0437	0.58uM	59.0%@1.0uM		
B-0438	<0.1uM	91.0%@1.0uM		
B-0439	2.12uM	65.0%@1.0uM		
B-0440	0.66uM	63.0%@1.0uM		
B-0441	0.8uM	58.0%@1.0uM		
B-0442	<0.1uM	91.0%@1.0uM		
B-0443	2.01uM	71.0%@1.0uM		
B-0444	1.01uM	51.0%@1.0uM		
B-0445	<0.1uM	83.0%@1.0uM		
B-0446	0.78uM	80.0%@1.0uM		
B-0447	0.19uM	71.0%@1.0uM		
B-0448	0.4uM	79.0%@1.0uM		
B-0449	0.83uM	81.0%@1.0uM		
B-0450	0.26uM	81.0%@1.0uM		
B-0451	0.071uM	83.0%@1.0uM	42%@30mpk@-6h	
B-0452	0.7uM	75.0%@1.0uM		
B-0453	0.47uM	75.0%@1.0uM		
B-0454	0.11uM	80.0%@1.0uM		
B-0455	<0.1uM	95.0%@1.0uM		36%@3mpk@-4h
B-0456	1.81uM	67.0%@1.0uM		
B-0457	0.089uM	81.0%@1.0uM		
B-0458	0.033uM	70.0%@1.0uM		
B-0459	0.099uM	76.0%@1.0uM		
B-0460	0.061uM	92.0%@1.0uM		
B-0461	0.025uM	96.0%@1.0uM		
B-0462	<0.1uM	97.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0463	0.052uM	95.0%@1.0uM		
B-0464	<0.1uM	91.0%@1.0uM		
B-0465	0.084uM	98.0%@1.0uM		
B-0466	<0.1uM	98.0%@1.0uM		0%@3mpk@-4h
B-0467	<0.1uM	77.0%@1.0uM		
B-0468	0.031uM	93.0%@1.0uM		
B-0469	0.056uM	92.0%@1.0uM		
B-0470	0.063uM	92.0%@1.0uM		
B-0471	0.027uM	97.0%@1.0uM		
B-0472	0.19uM	54.0%@1.0uM		
B-0473	0.004uM	95.0%@1.0uM		
B-0474	0.024uM	86.0%@1.0uM		
B-0475	0.21uM	74.0%@1.0uM		
B-0476	0.56uM	69.0%@1.0uM		
B-0477	1.48uM	96.0%@1.0uM		
B-0478	0.034uM	87.0%@1.0uM		
B-0479	0.031uM	90.0%@1.0uM		15%@3mpk@-4h
B-0480	0.12uM	88.0%@1.0uM		
B-0481	0.014uM	95.0%@1.0uM		56%@3mpk@-4h
B-0482	0.97uM	68.0%@1.0uM		
B-0483	0.57uM	68.0%@1.0uM		
B-0484	0.28uM	62.0%@1.0uM		
B-0485	0.04uM	95.0%@1.0uM		
B-0486	0.24uM	80.0%@1.0uM		
B-0487	0.11uM	89.0%@1.0uM		54%@3mpk@-4h
B-0488	0.62uM	88.0%@1.0uM		
B-0489	0.3uM	80.0%@1.0uM		
B-0490	0.91uM	74.0%@1.0uM		
B-0491	0.43uM	66.0%@1.0uM		
B-0492	0.069uM	42.0%@1.0uM		
B-0493	0.3uM	36.0%@1.0uM		
B-0494	0.13uM	30.0%@1.0uM		
B-0495	0.12uM	25.0%@1.0uM		
B-0496	0.83uM	16.0%@1.0uM		
B-0497	0.44uM	31.0%@1.0uM		
B-0498	0.33uM	11.0%@1.0uM		
B-0499	0.39uM	37.0%@1.0uM		
B-0500	0.26uM	41.0%@1.0uM		
B-0501	0.049uM	52.0%@1.0uM		
B-0502	0.065uM	48.0%@1.0uM		
B-0503	0.16uM	73.0%@1.0uM		
B-0504	0.4uM	43.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0505	0.28uM	44.0%@1.0uM		
B-0506	0.94uM	43.0%@1.0uM		
B-0507	0.18uM	75.0%@1.0uM		
B-0508	2.0uM	48.0%@1.0uM		
B-0509	0.1uM	86.0%@1.0uM		
B-0510	0.69uM	61.0%@1.0uM		
B-0511	0.007uM	90.0%@1.0uM		
B-0512	1.0uM	53.0%@1.0uM		
B-0513	0.72uM	52.0%@1.0uM		
B-0514	0.14uM	87.0%@1.0uM		
B-0515	0.42uM	61.0%@1.0uM		
B-0516	0.37uM	84.0%@1.0uM		
B-0517	0.094uM	52.0%@1.0uM		
B-0518	0.11uM	64.0%@1.0uM		
B-0519	0.043uM	87.0%@1.0uM		
B-0520	0.4uM	67.0%@1.0uM		
B-0521	1.37uM	52.0%@1.0uM		
B-0522	0.15uM	75.0%@1.0uM		
B-0523	0.19uM	83.0%@1.0uM		
B-0524	0.4uM	77.0%@1.0uM		
B-0525	0.16uM	76.0%@1.0uM		
B-0526	0.031uM	87.0%@1.0uM		
B-0527	1.09uM	63.0%@1.0uM		
B-0528	0.14uM	70.0%@1.0uM		
B-0529	0.11uM	73.0%@1.0uM		
B-0530	5.53uM	45.0%@1.0uM		
B-0531	0.5uM	48.0%@1.0uM		
B-0532	0.45uM	1.01uM	41%@30mpk@-6h	
B-0533	1.23uM	47.0%@1.0uM		
B-0534	0.41uM	54.0%@1.0uM		
B-0535	0.44uM	0.87uM		
B-0536	0.46uM	0.15uM		
B-0537	3.44uM	51.0%@1.0uM		
B-0538	1.13uM	45.0%@1.0uM		
B-0539	2.84uM	21.0%@1.0uM		
B-0540	3.62uM	54.0%@1.0uM		
B-0541	3.24uM	28.0%@1.0uM		
B-0542	1.55uM	50.0%@1.0uM		
B-0543	1.56uM	43.0%@1.0uM		
B-0544	1.12uM	27.0%@1.0uM		
B-0545	1.06uM	41.0%@1.0uM		
B-0546	1.04uM	18.0%@1.0uM		
B-0547	1.24uM	21.0%@1.0uM		
B-0548	1.77uM	28.0%@1.0uM		
B-0549	2.22uM	22.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0550	2.41uM	14.0% @1.0uM		
B-0551	1.08uM	56.0% @1.0uM		
B-0552	0.13uM	46.0% @1.0uM		
B-0553	1.44uM	47.0% @1.0uM		
B-0554	2.58uM	20.0% @1.0uM		
B-0555	1.87uM	34.0% @1.0uM		
B-0556	0.49uM	39.0% @1.0uM		
B-0557	1.37uM	32.0% @1.0uM		
B-0558	0.85uM	33.0% @1.0uM		
B-0559	0.53uM	49.0% @1.0uM		
B-0560	2.57uM	31.0% @1.0uM		
B-0561	2.07uM	40.0% @1.0uM		
B-0562	0.22uM	0.3uM		5% @3mpk@-4h
B-0563	0.18uM	0.13uM		
B-0564	0.82uM	58% @1.0uM		
B-0565	0.23uM	0.59uM		
B-0566	<0.1uM	0.17uM		0% @3mpk@-4h
B-0567	0.14uM	0.28uM		
B-0568	1.22uM	46.0% @1.0uM		
B-0569	0.15uM	0.26uM		
B-0570	0.27uM	46.0% @1.0uM		
B-0571	0.38uM	44.0% @1.0uM		
B-0572	0.27uM	41.0% @1.0uM		
B-0573	0.36uM	1.7uM		
B-0574	0.13uM	0.66uM		37% @3mpk@-4h
B-0575	0.032uM	0.17uM		
B-0576	0.068uM	0.39uM		65% @3mpk@-4h
B-0577	0.091uM	66.0% @1.0uM		
B-0578	1.88uM	47.0% @1.0uM		
B-0579	0.11uM	79.0% @1.0uM		
B-0580	2.23uM	0.84uM		
B-0581	0.26uM	2.17uM		
B-0582	1.03uM	37.0% @1.0uM		
B-0583	3.93uM	26.0% @1.0uM		
B-0584	0.66uM	54.0% @1.0uM		
B-0585	0.83uM	79.0% @1.0uM	50% @30mpk@-6h	
B-0586	0.81uM	51.0% @1.0uM		
B-0587	6.84uM	38% @1.0uM		
B-0588	12.8uM	42% @1.0uM		
B-0589	1.71uM	42% @1.0uM		
B-0590	1.57uM	38.0uM		
B-0591	3.59uM	29.0% @1.0uM		
B-0592	1.62uM	45.0% @1.0uM		
B-0593	1.22uM	36.0% @1.0uM		
B-0594	-	41.0% @1.0uM		
B-0595	2.42uM	22.0% @1.0uM		
B-0596	20.0uM	41.0% @1.0uM		
B-0597	1.68uM	63.0% @1.0uM		
B-0598	2.12uM	50.0% @1.0uM		



Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0599	4.16uM	21.0%@1.0uM		
B-0600	0.002uM	28.0%@1.0uM		
B-0601	0.089uM	1.31uM		43%@3mpk%-4h
B-0602	0.97uM	61.0%@1.0uM		
B-0603	0.09uM	51.0%@1.0uM		
B-0604	0.3uM	20.0%@1.0uM		
B-0605	0.18uM	47.0%@1.0uM		
B-0606	0.17uM	53.0%@1.0uM		
B-0607	2.79uM	70.0%@1.0uM		
B-0608	0.059uM	73.0%@1.0uM		
B-0609	<0.1uM	87.0%@1.0uM		
B-0610	<0.1uM	88.0%@1.0uM		
B-0611	0.65uM	60.0%@1.0uM		
B-0612	0.16uM	60.0%@1.0uM		
B-0613	0.17uM	76.0%@1.0uM		
B-0614	0.76uM	70.0%@1.0uM		0%@3mpk@-4h
B-0615	0.08uM	83.0%@1.0uM		
B-0616	0.38uM	87.0%@1.0uM		
B-0617	0.045uM	92.0%@1.0uM		
B-0618	0.37uM	80.0%@1.0uM		
B-0619	<0.1uM	88.0%@1.0uM		
B-0620	1.59uM	58.0%@1.0uM		
B-0621	0.36uM	68.0%@1.0uM		
B-0622	0.076uM	78.0%@1.0uM		
B-0623	0.12uM	76.0%@1.0uM		
B-0624	0.085uM	54.0%@1.0uM		
B-0625	0.023uM	88.0%@1.0uM		
B-0626	<0.1uM	85.0%@1.0uM		
B-0627	0.25uM	69.0%@1.0uM		
B-0628	0.023uM	72.0%@1.0uM		
B-0629	0.2uM	79.0%@1.0uM		
B-0630	0.06uM	77.0%@1.0uM		
B-0631	0.065uM	81.0%@1.0uM		
B-0632	<0.1uM	79.0%@1.0uM		
B-0633	0.6uM	80.0%@1.0uM		
B-0634	0.6uM	40.0%@1.0uM		
B-0635	0.15uM	55.0%@1.0uM		
B-0636	<0.1uM	86.0%@1.0uM		
B-0637	0.11uM	92.0%@1.0uM		
B-0638	0.25uM	89.0%@1.0uM		
B-0639	0.051uM	93.0%@1.0uM		50%@3mpk@-4h
B-0640	0.36uM	94.0%@1.0uM		
B-0641	0.58uM	65.0%@1.0uM		
B-0642	0.49uM	90.0%@1.0uM		
B-0643	0.069uM	85.0%@1.0uM		0%@3mpk@-4h
B-0644	0.058uM	89.0%@1.0uM		
B-0645	0.58uM	80.0%@1.0uM		
B-0646	0.26uM	94.0%@1.0uM		
B-0647	1.61uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0648	<0.1uM	83.0%@1.0uM		
B-0649	0.83uM	39.0%@1.0uM		
B-0650	0.006uM	95.0%@1.0uM		8%@3mpk@-4h
B-0651	1.78uM	81.0%@1.0uM		
B-0652	0.19uM	83.0%@1.0uM		
B-0653	2.01uM	74.0%@1.0uM		
B-0654	5.97uM	78.0%@1.0uM		
B-0655	1.25uM	76.0%@1.0uM		
B-0656	0.007uM	95.0%@1.0uM		28%@3mpk@-4h
B-0657	0.17uM	83.0%@1.0uM		
B-0658	1.14uM	91.0%@1.0uM		
B-0659	2.64uM	87.0%@1.0uM		
B-0660	0.088uM	92.0%@1.0uM		
B-0661	<0.1uM	90.0%@1.0uM		
B-0662	<0.1uM	95.0%@1.0uM		
B-0663	0.88uM	74.0%@1.0uM		
B-0664	0.39uM	80.0%@1.0uM		
B-0665	0.47uM	72.0%@1.0uM		
B-0666	0.17uM	73.0%@1.0uM		
B-0667	0.83uM	75.0%@1.0uM		
B-0668	0.27uM	78.0%@1.0uM		
B-0669	0.89uM	34.0%@1.0uM		
B-0670	3.15uM	32.0%@1.0uM		
B-0671	6.38uM	36.0%@1.0uM		
B-0672	6.59uM	32.0%@1.0uM		
B-0673	8.54uM	48.0%@1.0uM		
B-0674	2.81uM	42.0%@1.0uM		
B-0675	5.42uM	3.0%@1.0uM		
B-0676	2.09uM	22.0%@1.0uM		
B-0677	1.63uM	25.0%@1.0uM		
B-0678	0.38uM	52.0%@1.0uM		
B-0679	0.062uM	45.0%@1.0uM		
B-0680	0.42uM	67.0%@1.0uM		
B-0681	1.96uM	17.0%@1.0uM		
B-0682	0.76uM	39.0%@1.0uM		
B-0683	13.0uM	32.0%@1.0uM		
B-0684	0.54uM	68.0%@1.0uM		
B-0685	15.4uM	33.0%@1.0uM		
B-0686	0.42uM	59.0%@1.0uM		
B-0687	10.1uM	15.0%@1.0uM		
B-0688	0.66uM	58.0%@1.0uM		
B-0689	14.6uM	27.0%@1.0uM		
B-0690	27.1uM	36.0%@1.0uM		
B-0691	0.16uM	48.0%@1.0uM		
B-0692	0.38uM	29.0%@1.0uM		
B-0693	0.39uM	28.0%@1.0uM		
B-0694	0.62uM	21.0%@1.0uM		
B-0695	0.23uM	32.0%@1.0uM		
B-0696	0.085uM	35.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0697	0.45uM	44.0%@1.0uM		
B-0698	2.33uM	43.0%@1.0uM		
B-0699	0.34uM	31.0%@1.0uM		
B-0700	0.24uM	56.0%@1.0uM		
B-0701	0.39uM	45.0%@1.0uM		
B-0702	0.036uM	39.0%@1.0uM		
B-0703	0.12uM	39.0%@1.0uM		
B-0704	2.19uM	29.0%@1.0uM		
B-0705	0.44uM	21.0%@1.0uM		
B-0706	0.44uM	32.0%@1.0uM		
B-0707	1.7uM			
B-0708	2.1uM			
B-0709	0.84uM			
B-0710	1.99uM			
B-0711	1.99uM			
B-0712	2.9uM			
B-0713	4.3uM			
B-0714	3.7uM			
B-0715	3.2uM			
B-0716	4.6uM			
B-0717	4.3uM			
B-0718	1.4uM			
B-0719	3.4uM			
B-0720	1.3uM			
B-0721	3.8uM			
B-0722	0.07uM	>1.0uM		
B-0723	0.47uM			
B-0724	0.06uM	17.0%@1.0uM		
B-0725	9.7uM			
B-0726	1.4uM			
B-0727	0.51uM			
B-0728	20.0uM			
B-0729	0.87uM			
B-0730	0.25uM	11.0%@1.0uM		
B-0731	0.87uM	>1.0uM		
B-0732	14.0uM			
B-0733	32.0uM			
B-0734	0.92uM			
B-0735	1.0uM			
B-0736	26.0uM			
B-0737	2.6uM			
B-0738	2.7uM			
B-0739	4.1uM			
B-0740	4.4uM			
B-0741	26.0uM			
B-0742	2.2uM			
B-0743	1.2uM			
B-0744	23.0uM			
B-0745	6.0uM			

1030

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0746	0.01uM	22.0%@1.0uM		
B-0747	1.1uM			
B-0748	1.2uM			
B-0749	4.4uM			
B-0750	0.92uM			
B-0751	1.6uM			
B-0752	0.33uM			
B-0753	0.37uM			
B-0754	0.55uM			
B-0755	2.3uM			
B-0756	0.94uM			
B-0757	0.54uM	16.0%@1.0uM		
B-0758	1.5uM			
B-0759	0.3uM			
B-0760	0.01uM	13.0%@1.0uM		
B-0761	<0.1uM			
B-0762	0.13uM	5.0%@1.0uM		
B-0763	0.015uM	17.0%@1.0uM		
B-0764	0.67uM	26.0%@1.0uM		
B-0765	0.3uM	29.0%@1.0uM		
B-0766	0.95uM			
B-0767	0.08uM			
B-0768	1.4uM			
B-0769	12.7uM			
B-0770	2.3uM			
B-0771	0.5uM			
B-0772	0.8uM			
B-0773	14.0uM			
B-0774	1.5uM			
B-0775	0.6uM	>1.0uM		
B-0776	0.9uM	>1.0uM		
B-0777	21.0uM			
B-0778	51.0uM			
B-0779	0.5uM			
B-0780	1.1uM			
B-0781	48.0uM			
B-0782	22.0uM			
B-0783	8.0uM			
B-0784	7.0uM			
B-0785	23.0uM			
B-0786	24.0uM			
B-0787	1.5uM			
B-0788	1.2uM			
B-0789	33.0uM			
B-0790	1.0uM	4.0%@1.0uM		
B-0791	0.3uM	>1.0uM		
B-0792	1.1uM			
B-0793	0.3uM			
B-0794	2.9uM	2.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0795	1.9uM	11.0%@1.0uM		
B-0796	1.4uM			
B-0797	1.04uM	-		
B-0798	1.73uM	-		
B-0799	-	>1.0uM		
B-0800	1.01uM	>1.0uM		
B-0801	0.67uM	>1.0uM		
B-0802	-	>1.0uM		
B-0803	0.057uM	53.0%@1.0uM		
B-0804	0.3uM	32.0%@1.0uM		
B-0805	0.71uM	>1.0uM		
B-0806	3.28uM	>1.0uM		
B-0807	10.8uM	-		
B-0808	3.09uM	>1.0uM		
B-0809	1.22uM	7.0%@1.0uM		
B-0810	1.11uM	>1.0uM		
B-0811	2.79uM	2.0%@1.0uM		
B-0812	2.12uM	>1.0uM		
B-0813	3.02uM	>1.0uM		
B-0814	-	>1.0uM		
B-0815	2.11uM	>1.0uM		
B-0816	3.46uM	>1.0uM		
B-0817	3.07uM	33.0%@1.0uM		
B-0818	4.97uM	>1.0uM		
B-0819	1.08uM	>1.0uM		
B-0820	1.64uM	3.0%@1.0uM		
B-0821	1.44uM	-		
B-0822	1.33uM	-		
B-0823	2.39uM	>1.0uM		
B-0824	3.41uM	-		
B-0825	-	-		
B-0826	1.74uM	-		
B-0827	15.6uM	-		
B-0828	7.9uM	-		
B-0829	0.61uM	65.0%@1.0uM		
B-0830	0.54uM	34.0%@1.0uM		
B-0831	0.9uM	>1.0uM		
B-0832	1.49uM	-		
B-0833	0.95uM	23.0%@1.0uM		
B-0834	1.25uM	-		
B-0835	-	-		
B-0836	1.24uM	-		
B-0837	1.96uM	>1.0uM		
B-0838	3.1uM	-		
B-0839	4.3uM	-		
B-0840	0.63uM	47.0%@1.0uM		
B-0841	0.32uM	36.0%@1.0uM		
B-0842	0.74uM	63.0%@1.0uM		
B-0843	0.61uM	>1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0844	0.4uM	25.0%@1.0uM		
B-0845	1.78uM	-		
B-0846	1.8uM	-		
B-0847	0.73uM	21.0%@1.0uM		
B-0848	1.56uM	-		
B-0849	1.25uM	-		
B-0850	1.81uM	-		
B-0851	0.91uM	39.0%@1.0uM		
B-0852	1.02uM	-		
B-0853	-	38.0%@1.0uM		
B-0854	-	25.0%@1.0uM		
B-0855	-	8.0%@1.0uM		
B-0856	-	38.0%@1.0uM		
B-0857	6.25uM	-		
B-0858	2.1uM	48.0%@1.0uM		
B-0859	39.5uM	-		
B-0860	38.1uM	-		
B-0861	1.32uM	12.0%@1.0uM		
B-0862	2.15uM	4.0%@1.0uM		
B-0863	0.81uM	25.0%@1.0uM		
B-0864	0.39uM	40.0%@1.0uM		
B-0865	0.66uM	46.0%@1.0uM		
B-0866	1.38uM	28.0%@1.0uM		
B-0867	0.62uM	>1.0uM		
B-0868	3.28uM	8.0%@1.0uM		
B-0869	4.19uM	>1.0uM		
B-0870	3.13uM	>1.0uM		
B-0871	1.9uM	>1.0uM		
B-0872	3.13uM	3.0%@1.0uM		
B-0873	6.92uM	>1.0uM		
B-0874	1.92uM	>1.0uM		
B-0875	2.13uM	8% @1.0uM		
B-0876	0.89uM	>1.0uM		
B-0877	1.17uM	13.0%@1.0uM		
B-0878	0.65uM	19.0%@1.0uM		
B-0879	0.87uM	1.0%@1.0uM		
B-0880	0.15uM	40.0%@1.0uM		
B-0881	1.36uM	>1.0uM		
B-0882	1.48uM	9% @1.0uM		
B-0883	1.06uM	>1.0uM		
B-0884	1.89uM	-		
B-0885				
B-0886				
B-0887				
B-0888				
B-0889				
B-0890				
B-0891				
B-0892				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0893				
B-0894				
B-0895				
B-0896				
B-0897				
B-0898				
B-0899				
B-0900				
B-0901				
B-0902				
B-0903				
B-0904				
B-0905				
B-0906				
B-0907				
B-0908				
B-0909				
B-0910				
B-0911				
B-0912				
B-0913				
B-0914				
B-0915				
B-0916				
B-0917				
B-0918				
B-0919				
B-0920				
B-0921				
B-0922				
B-0923				
B-0924				
B-0925				
B-0926				
B-0927				
B-0928				
B-0929				
B-0930				
B-0931				
B-0932				
B-0933	47.0%@1.0uM	37.0%@1.0uM		
B-0934	67.0%@1.0uM	36.0%@1.0uM		
B-0935	69.0%@1.0uM	54.0%@1.0uM		
B-0936	69.0%@1.0uM	>1.0uM		
B-0937	64.0%@1.0uM	1.74uM		
B-0938	51.0%@1.0uM	29.0%@1.0uM		
B-0939	78.0%@1.0uM	14.0%@1.0uM		
B-0940	56.0%@1.0uM	22.0%@1.0uM		
B-0941	81.0%@1.0uM	25.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0942	82.0% @ 1.0uM	2.0% @ 1.0uM		
B-0943	63.0% @ 10.0uM	24.0% @ 1.0uM		
B-0944	45.0% @ 1.0uM	27.0% @ 1.0uM		
B-0945	96.0% @ 1.0uM	0.93uM		
B-0946	76.0% @ 1.0uM	31.0% @ 1.0uM		
B-0947	69.0% @ 1.0uM	34.0% @ 1.0uM		
B-0948	68.0% @ 1.0uM	1.81uM		
B-0949	90.0% @ 1.0uM	17.0% @ 1.0uM		
B-0950	81.0% @ 1.0uM	0.58uM		
B-0951	82.0% @ 1.0uM	20.0% @ 1.0uM		
B-0952	44.0% @ 1.0uM	21.0% @ 1.0uM		
B-0953	63.0% @ 1.0uM	25.0% @ 1.0uM		
B-0954	62.0% @ 1.0uM	0.52uM		
B-0955	49.0% @ 1.0uM	0.54uM		
B-0956	56.0% @ 1.0uM	1.33uM		
B-0957	79.0% @ 1.0uM	22.0% @ 1.0uM		
B-0958	74.0% @ 1.0uM	0.38uM		
B-0959	83.0% @ 1.0uM	39.0% @ 1.0uM		
B-0960	48.0% @ 1.0uM	4.0% @ 1.0uM		
B-0961	79.0% @ 1.0uM	23.0% @ 1.0uM		
B-0962	85.0% @ 1.0uM	2.71uM		
B-0963	76.0% @ 1.0uM	39.0% @ 1.0uM		
B-0964	94.0% @ 1.0uM	5.0uM		
B-0965	74.0% @ 1.0uM	1.1uM		
B-0966	50.0% @ 1.0uM	5.0% @ 1.0uM		
B-0967	80.0% @ 1.0uM	29.0% @ 1.0uM		
B-0968	35.0% @ 1.0uM	26.0% @ 1.0uM		
B-0969	63.0% @ 1.0uM	35.0% @ 1.0uM		
B-0970	76.0% @ 10.0uM	0.88uM		
B-0971	61.0% @ 1.0uM	39.0% @ 1.0uM		
B-0972	85.0% @ 1.0uM	2.0% @ 1.0uM		
B-0973	66.0% @ 10.0uM	48.0% @ 1.0uM		
B-0974	57.0% @ 1.0uM	47.0% @ 1.0uM		
B-0975	82.0% @ 1.0uM	32.0% @ 1.0uM		
B-0976	79.0% @ 1.0uM	36.0% @ 1.0uM		
B-0977	60.0% @ 1.0uM	26.0% @ 1.0uM		
B-0978	59.0% @ 1.0uM	36.0% @ 1.0uM		
B-0979	56.0% @ 10.0uM	23.0% @ 1.0uM		
B-0980	68.0% @ 1.0uM	31.0% @ 1.0uM		
B-0981	62.0% @ 1.0uM	57.0% @ 1.0uM		
B-0982	65.0% @ 1.0uM	23.0% @ 1.0uM		
B-0983	75.0% @ 1.0uM	0.8uM		
B-0984	60.0% @ 1.0uM	51.0% @ 1.0uM		
B-0985	86.0% @ 1.0uM	0.75uM		
B-0986	70.0% @ 1.0uM	71.0% @ 1.0uM		
B-0987	78.0% @ 1.0uM	79.0% @ 1.0uM		
B-0988	72.0% @ 1.0uM	65.0% @ 1.0uM		
B-0989	85.0% @ 1.0uM	0.85uM		
B-0990	-	26.0% @ 1.0uM		



Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0991	58.0%@1.0uM	33.0%@1.0uM		
B-0992	77.0%@1.0uM	45.0%@1.0uM		
B-0993	57.0%@1.0uM	73.0%@1.0uM		
B-0994	55.0%@1.0uM	43.0%@1.0uM		
B-0995	53.0%@1.0uM	14.0%@1.0uM		
B-0996	54.0%@1.0uM	27.0%@1.0uM		
B-0997	69.0%@1.0uM	22.0%@1.0uM		
B-0998	67.0%@1.0uM	25.0%@1.0uM		
B-0999	61.0%@1.0uM	24.0%@1.0uM		
B-1000	55.0%@1.0uM	42.0%@1.0uM		
B-1001	63.0%@1.0uM	31.0%@1.0uM		
B-1002	70.0%@1.0uM	41.0%@1.0uM		
B-1003	74.0%@1.0uM	29.0%@1.0uM		
B-1004	79.0%@1.0uM	45.0%@1.0uM		
B-1005	58.0%@1.0uM	23.0%@1.0uM		
B-1006	69.0%@1.0uM	38.0%@1.0uM		
B-1007	52.0%@1.0uM	34.0%@1.0uM		
B-1008	54.0%@1.0uM	23.0%@1.0uM		
B-1009	80.0%@1.0uM	55.0%@1.0uM		
B-1010	75.0%@1.0uM	1.0uM		
B-1011	72.0%21.0uM	17.0%@1.0uM		
B-1012	-	20.0%@1.0uM		
B-1013	85.0%@1.0uM	7.0%@1.0uM		
B-1014	88.0%@1.0uM	20.0%@1.0uM		
B-1015	77.0%@1.0uM	34.0%@1.0uM		
B-1016	58.0%@1.0uM	10.0%@1.0uM		
B-1017	96.0%@1.0uM	58.0%@1.0uM		
B-1018	88.0%@1.0uM	34.0%@1.0uM		
B-1019	82.0%@1.0uM	66.0%@1.0uM		
B-1020	87.0%@1.0uM	36.0%@1.0uM		
B-1021	82.0%@1.0uM	35.0%@1.0uM		
B-1022	84.0%@1.0uM	53.0%@1.0uM		
B-1023	93.0%@1.0uM	70.0%@1.0uM		
B-1024	89.0%@1.0uM	57.0%@1.0uM		
B-1025	61.0%@1.0uM	23.0%@1.0uM		
B-1026	87.0%@1.0uM	53.0%@1.0uM		
B-1027	58.0%@1.0uM	18.0%@1.0uM		
B-1028	70.0%@1.0uM	17.0%@1.0uM		
B-1029	69.0%@1.0uM	54.0%@1.0uM		
B-1030	76.0%@1.0uM	60.0%@1.0uM		
B-1031	69.0%@1.0uM	42.0%@1.0uM		
B-1032	76.0%@1.0uM	37.0%@1.0uM		
B-1033	86.0%@1.0uM	34.0%@1.0uM		
B-1034	66.0%@1.0uM	39.0%@1.0uM		
B-1035	75.0%@1.0uM	52.0%@1.0uM		
B-1036	68.0%@1.0uM	68.0%@1.0uM		
B-1037	-	41.0%@1.0uM		
B-1038	57.0%@1.0uM	0.57uM		
B-1039	-	1.33uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1040	72.0%@1.0uM	0.38uM		
B-1041	70.0%@1.0uM	73.0%@1.0uM		
B-1042	79.0%@1.0uM	12.0%@1.0uM		
B-1043	64.0%@1.0uM	53.0%@1.0uM		
B-1044	94.0%@1.0uM	0.93uM		
B-1045	78.0%@1.0uM	25.0%@1.0uM		
B-1046	72.0%@1.0uM	66.0%@1.0uM		
B-1047	72.0%@1.0uM	58.0%@1.0uM		
B-1048	67.0%@1.0uM	19.0%@1.0uM		
B-1049	67.0%@1.0uM	65.0%@1.0uM		
B-1050	-	0.54uM		
B-1051	68.0%@1.0uM	41%@1.0uM		
B-1052	69.0%@1.0uM	66%@1.0uM		
B-1053	78.0%@1.0uM	0.4uM		
B-1054	79.0%@1.0uM	55.0%@1.0uM		
B-1055	89.0%@1.0uM	63.0%@1.0uM		
B-1056	89.0%@1.0uM	0.76uM		
B-1057	85.0%@1.0uM	0.72uM		
B-1058	0.66uM	43.0%@1.0uM		
B-1059	0.18uM	24.0%@1.0uM		
B-1060	0.11uM	32.0%@1.0uM		
B-1061	0.03uM	19.0%@1.0uM		
B-1062	<0.1uM	26.0%@1.0uM		
B-1063	0.16uM	44.0%@1.0uM		
B-1064	0.39uM	50.0%@1.0uM		
B-1065	0.56uM	40.0%@1.0uM		
B-1066	<0.1uM	39.0%@1.0uM		
B-1067	1.6uM	32.0%@1.0uM		
B-1068	0.48uM	24.0%@1.0uM		
B-1069	0.22uM	27.0%@1.0uM		
B-1070	<0.1uM	44.0%@1.0uM		
B-1071	<0.1uM	48.0%@1.0uM		
B-1072	0.38uM	28.0%@1.0uM		
B-1073	<0.1uM	21.0%@1.0uM		
B-1074	0.23uM	33.0%@1.0uM		
B-1075	0.03uM	29.0%@1.0uM		
B-1076	0.08uM	31.0%@1.0uM		
B-1077	<0.1uM	38.0%@1.0uM		
B-1078	0.26uM	48.0%@1.0uM		
B-1079	<0.1uM	40.0%@1.0uM		
B-1080	0.19uM	28.0%@1.0uM		
B-1081	<0.1uM	37.0%@1.0uM		
B-1082	<0.1uM	54.0%@1.0uM		
B-1083	<0.1uM	23.0%@1.0uM		
B-1084	0.43uM	29.0%@1.0uM		
B-1085	<0.1uM	29.0%@1.0uM		
B-1086	<0.1uM	42.0%@1.0uM		
B-1087	0.05uM	32.0%@1.0uM		
B-1088	0.73uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1089	<0.1uM	39.0%@1.puM		
B-1090	<0.1uM	90.0%@1.0uM		
B-1091	<0.1uM	73.0%@1.0uM		
B-1092	0.27uM	85.0%@1.0uM		
B-1093	0.33uM	36.0%@1.0uM		
B-1094	0.013uM	69.0%@1.0uM		
B-1095	<0.1uM	70.0%@1.0uM		
B-1096	<0.1uM	32.0%@1.0uM		
B-1097	<0.1uM	44.0%@1.07uM		
B-1098	<0.1uM	82.0%@1.0uM		
B-1099	0.26uM	74.0%@1.0uM		
B-1100	0.22uM	56.0%@1.0uM		
B-1101	0.026uM	82.0%@1.0uM		
B-1102	0.035uM	83.0%@1.0uM		
B-1103	0.094uM	90.0%@1.0uM		
B-1104	0.12uM	69.0%@1.0uM		
B-1105	<0.1uM	84.0%@1.0uM		
B-1106	<0.1uM	86.0%@1.0uM		
B-1107	0.057uM	84.0%@1.0uM		
B-1108	0.22uM	81.0%@1.0uM		
B-1109	0.054uM	80.0%@1.0uM		
B-1110	0.47uM	64.0%@1.0uM		
B-1111	0.19uM	64.0%@1.0uM		
B-1112	0.58uM	43.0%@1.0uM		
B-1113	<0.1uM	72.0%@1.0uM		
B-1114	0.069uM	51.0%@1.0uM		
B-1115	0.024uM	89.0%@1.0uM		
B-1116	0.41uM	81.0%@1.0uM		
B-1117	0.13uM	73.0%@1.0uM		
B-1118	0.33uM	91.0%@1.0uM		
B-1119	0.35uM	80.0%@1.0uM		
B-1120	0.47uM	9.0%@1.0uM		
B-1121	3.58uM	29.0%@1.0uM		
B-1122	1.84uM	32.0%@1.0uM		
B-1123	2.93uM	27.0%@1.0uM		
B-1124	1.49uM	52.0%@1.0uM		
B-1125	0.56uM	41.0%@1.0uM		
B-1126	1.5uM	>1.0uM		
B-1127	0.71uM	7.0%@1.0uM		
B-1128	2.55uM	26.0%@1.0uM		
B-1129	1.07uM	46.0%@1.0uM		
B-1130	0.5uM	29.0%@1.0uM		
B-1131	0.076uM	34.0%@1.0uM		
B-1132	0.72uM	11.0%@1.0uM		
B-1133	0.38uM	33.0%@1.0uM		
B-1134	1.71uM	33.0%@1.0uM		
B-1135	0.23uM	38.0%@1.0uM		
B-1136	1.17uM	40.0%@1.0uM		
B-1137	0.038uM	35.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1138	1.82uM	>1.0uM		
B-1139	0.041uM	29.0%@1.0uM		
B-1140	1.68uM	39.0%@1.0uM		
B-1141	2.47uM	32.0%@1.0uM		
B-1142	0.11uM	37.0%@1.0uM		
B-1143	0.17uM	40.0%@1.0uM		
B-1144	0.44uM	72.0%@1.0uM		
B-1145	1.07uM	71.0%@1.0uM		
B-1146	0.47uM	61.0%@1.0uM		
B-1147	0.095uM	53.0%@1.0uM		
B-1148	0.43uM	61.0%@1.0uM		
B-1149	1.55uM	48.0%@1.0uM		
B-1150	0.47uM	75.0%@1.0uM		
B-1151	0.32uM	72.0%@1.0uM		
B-1152	0.73uM	53.0%@1.0uM		
B-1153	2.22uM	52.0%@1.0uM		
B-1154	0.085uM	46.0%@1.0uM		
B-1155	3.22uM	30.0%@1.0uM		
B-1156	0.27uM	78.0%@1.0uM		
B-1157	0.26uM	66.0%@1.0uM		
B-1158	74%@1.0uM	0.68uM	53%@30mpk@-6h	
B-1159	66.0%@1.0uM	1.03uM	60%@30mpk@-6h	
B-1160	79.0%@1.0uM	0.38uM		
B-1161	64.0%21.0uM	0.93uM	40%@30mpk@-6h	45%@3mpk@-4h
B-1162	79.0%@1.0uM	0.59uM	40%@30mpk@-6h	
B-1163	74.0%@1.0uM	0.37uM		
B-1164	-	0.35uM		
B-1165	66.0%@1.0uM	0.99uM		
B-1166	77.0%@1.0uM	0.39uM	50%@30mpk@-6h	50%@3mpk@-4h
B-1167	70.0%@1.0uM	1.06uM		
B-1168	66.0%@1.0uM	0.63uM		
B-1169	80.0%@1.0uM	0.11uM		
B-1170	82.0%@1.0uM	0.57uM		
B-1171	78.0%@1.0uM	0.23uM		
B-1172	68.0%@1.0uM	1.95uM		
B-1173	65.0%@1.0uM	62%@1.0uM		
B-1174	80.0%@1.0uM	0.86uM		
B-1175	72.0%@1.0uM	1.83uM		
B-1176	67.0%@1.0uM	67.0%@1.0uM		
B-1177	70.0%@1.0uM	1.16uM		
B-1178	92.0%@1.0uM	1.61uM		
B-1179	86.0%@1.0uM	0.41uM		
B-1180	78.0%@1.0uM	0.53uM		
B-1181	79.0%@1.0uM	66%@1.0uM		
B-1182	72.0%@1.0uM	0.65uM		
B-1183	77.0%@1.0uM	0.2uM		
B-1184	69.0%@1.0uM	0.63uM		
B-1185	71.0%@1.0uM	0.79uM		
B-1186	83.0%@1.0uM	60%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1187	76.0%@1.0uM	1.89uM		
B-1188	-	36.0%@1.0uM		
B-1189	68.0%@1.0uM	0.83uM		
B-1190	78.0%@1.0uM	62.0%@1.0uM		
B-1191	74.0%@1.0uM	57.0%@1.0uM		
B-1192	84.0%@1.0uM	0.47uM		
B-1193	69.0%@1.0uM	65.0%@1.0uM		
B-1194	87.0%@1.0uM	0.58uM		
B-1195	52.0%@1.0uM	60.0%@1.0uM		
B-1196	74.0%@1.0uM	68.0%@1.0uM		
B-1197	77.0%@1.0uM	45.0%@1.0uM		
B-1198	92.0%@1.0uM	0.46uM		
B-1199	87.0%@1.0uM	49.0%@1.0uM		
B-1200	95.0%@1.0uM	0.64uM		
B-1201	84.0%@1.0uM	0.51uM		
B-1202	71.0%@1.0uM	58.0%@1.0uM		
B-1203	84.0%@1.0uM	58.0%@1.0uM		
B-1204	68.0%@1.0uM	59.0%@1.0uM		
B-1205	74.0%@1.0uM	46.0%@1.0uM		
B-1206	81.0%@1.0uM	0.34uM		
B-1207	90.0%@1.0uM	58.0%@1.0uM		
B-1208	82.0%@1.0uM	51.0%@1.0uM		
B-1209	86.0%@1.0uM	55.0%@1.0uM		
B-1210	82.0%@1.0uM	57.0%@1.0uM		
B-1211	88.0%@1.0uM	59.0%@1.0uM		
B-1212	90.0%@1.0uM	57.0%@1.0uM		
B-1213	84.0%@1.0uM	0.62uM		
B-1214	76.0%@1.0uM	58.0%@1.0uM		
B-1215	86.0%@1.0uM	0.23uM		
B-1216	88.0%@1.0uM	0.18uM		
B-1217	87.0%@1.0uM	0.46uM		
B-1218	88.0%@1.0uM	76.0%@1.0uM		
B-1219	85.0%@1.0uM	37.0%@1.0uM		
B-1220	81.0%@1.0uM	53.0%@1.0uM		
B-1221	82.0%@1.0uM	44.0%@1.0uM		
B-1222	65.0%@1.0uM	9.0%@1.0uM		
B-1223	80.0%@1.0uM	61.0%@1.0uM		
B-1224	82.0%@1.0uM	74.0%@1.0uM		
B-1225	89.0%@1.0uM	73.0%@1.0uM		
B-1226	89.0%@1.0uM	0.18uM		
B-1227	83.0%@1.0uM	0.22uM		
B-1228	90.0%@1.0uM	0.72uM		
B-1229	87.0%@1.0uM	0.65uM		
B-1230	90.0%@1.0uM	0.25uM		
B-1231	94.0%@1.0uM	0.56uM		
B-1232	81.0%@1.0uM	54.0%@1.0uM		
B-1233	85.0%@1.0uM	0.36uM		
B-1234	89.0%@1.0uM	0.49uM		
B-1235	0.04uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1236	0.1uM	53.0%@1.0uM		
B-1237	0.22uM	39.0%@1.0uM		
B-1238	0.14uM	16.0%@1.0uM		
B-1239	<0.1uM	38.0%@1.0uM		
B-1240	<0.1uM	59.0%@1.0uM		
B-1241	0.04uM	81.0%@1.0uM		
B-1242	0.08uM	83.0%@1.0uM		
B-1243	0.04uM	47.0%@1.0uM		
B-1244	0.26uM	44.0%@1.0uM		
B-1245	0.49uM	42.0%@1.0uM		
B-1246	0.27uM	40.0%@1.0uM		
B-1247	<0.1uM	58.0%@1.0uM		
B-1248	<0.1uM	68.0%@1.0uM		
B-1249	0.24uM	60.0%@1.0uM		
B-1250	0.14uM	18.0%@1.0uM		
B-1251	0.41uM	38.0%@1.0uM		
B-1252	0.17uM	46.0%@1.0uM		
B-1253	0.15uM	57.0%@1.0uM		
B-1254	0.16uM	68.0%@1.0uM		
B-1255	12.9uM	75.0%@1.0uM		
B-1256	0.12uM	41.0%@1.0uM		
B-1257	1.48uM	40.0%@1.0uM		
B-1258	0.07uM	56.0%@1.0uM		
B-1259	<0.1uM	0.48uM		
B-1260	0.11uM	48.0%@1.0uM		
B-1261	0.74uM	44.0%@1.0uM		
B-1262	<0.1uM	63.0%@1.0uM		
B-1263	1.05uM	57.0%@1.0uM		
B-1264	0.32uM	47.0%@1.0uM		
B-1265	0.43uM	51.0%@1.0uM		
B-1266	<0.1uM	58.0%@1.0uM		
B-1267	<0.1uM	73.0%@1.0uM		
B-1268	<0.1uM	79.0%@1.0uM		
B-1269	0.46uM	84.0%@1.0uM		
B-1270	0.47uM	83.0%@1.0uM		
B-1271	0.13uM	74.0%@1.0uM		
B-1272	0.014uM	38.0%@1.0uM		
B-1273	<0.1uM	36.0%@1.0uM		
B-1274	<0.1uM	41.0%@1.0uM		
B-1275	<0.1uM	50.0%@1.0uM		
B-1276	0.062uM	11.0%@1.0uM		
B-1277	<0.1uM	47.0%@1.0uM		
B-1278	0.12uM	85.0%@1.0uM		
B-1279	<0.1uM	79.0%@1.0uM		
B-1280	0.039uM	83.0%@1.0uM		
B-1281	<0.1uM	85.0%@1.0uM		
B-1282	<0.1uM	75.0%@1.0uM		
B-1283	<0.1uM	64.0%@1.0uM		
B-1284	<0.1uM	75.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1285	0.057uM	80.0%@1.0uM		
B-1286	0.15uM	78.0%21.0uM		
B-1287	0.25uM	55.0%@1.0uM		
B-1288	0.15uM	74.0%@1.0uM		
B-1289	0.73uM	35.0%@1.0uM		
B-1290	0.26uM	75.0%@1.0uM		
B-1291	0.097uM	55.0%@1.0uM		
B-1292	0.01uM	74.0%@1.0uM		
B-1293	0.31uM	48.0%@1.0uM		
B-1294	0.013uM	54.0%@1.0uM		
B-1295	0.079uM	74.0%@1.0uM		
B-1296	0.038uM	48.0%@1.0uM		
B-1297	0.02uM	>1.0uM		
B-1298	0.055uM	20.0%@1.0uM		
B-1299	0.091uM	>1.0uM		
B-1300	0.071uM	18.0%@1.0uM		
B-1301	0.12uM	15.0%@1.0uM		
B-1302	0.023uM	11.0%@1.0uM		
B-1303	0.08uM	>1.0uM		
B-1304	0.11uM	10.0%@1.0uM		
B-1305	0.64uM	9.0%@1.0uM		
B-1306	0.11uM	>1.0uM		
B-1307	0.009uM	16.0%@1.0uM		
B-1308	<0.1uM	>1.0uM		
B-1309	0.045uM	>1.0uM		
B-1310	0.12uM	11.0%@1.0uM		
B-1311	0.05uM	57.0%@1.0uM		
B-1312	0.35uM	>1.0uM		
B-1313	0.035uM	37.0%@1.0uM		
B-1314	0.045uM	24.0%@1.0uM		
B-1315	0.055uM	12.0%@1.0uM		
B-1316	0.026uM	36.0%@1.0uM		
B-1317	0.019uM	9.0%@1.0uM		
B-1318	<0.1uM	1.0%@1.0uM		
B-1319	0.24uM	>1.0uM		
B-1320	0.047uM	43.0%@1.0uM		
B-1321	0.47uM	66.0%@1.0uM		
B-1322	0.12uM	87.0%@1.0uM		
B-1323	0.013uM	85.0%@1.0uM		
B-1324	0.16uM	83.0%@1.0uM		
B-1325	0.27uM	95.0%@1.0uM		
B-1326	0.092uM	84.0%@1.0uM		
B-1327	0.13uM	65.0%@1.0uM		
B-1328	0.032uM	86.0%@1.0uM		
B-1329	0.66uM	54.0%@1.0uM		
B-1330	0.053uM	85.0%@1.0uM		
B-1331	0.004uM	85.0%@1.0uM		
B-1332	0.007uM	81.0%@1.0uM		
B-1333	0.45uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1334	0.13uM	73.0%@1.0uM		
B-1335	0.097uM	63.0%@1.0uM		
B-1336	0.072uM	83.0%@1.0uM		
B-1337	0.4uM	90.0%@1.0uM		
B-1338	0.18uM	73.0%@1.0uM		
B-1339	0.12uM	67.0%@1.0uM		
B-1340	0.043uM	63.0%@1.0uM		
B-1341	0.42uM	52.0%@1.0uM		
B-1342	0.25uM	59.0%@1.0uM		
B-1343	0.065uM	83.0%@1.0uM		
B-1344	0.014uM	86.0%@1.0uM		
B-1345	0.27uM	73.0%@1.0uM		
B-1346	0.043uM	86.0%@1.0uM		
B-1347	0.021uM	84.0%@1.0uM		
B-1348	0.009uM	69.0%@1.0uM		
B-1349	0.037uM	86.0%@1.0uM		
B-1350	0.019uM	78.0%@1.0uM		
B-1351	0.068uM	78.0%@1.0uM		
B-1352	0.013uM	76.0%@1.0uM		
B-1353	0.062uM	80.0%@1.0uM		
B-1354	0.013uM	83.0%@1.0uM		
B-1355	0.07uM	75.0%@1.0uM		
B-1356	0.059uM	91.0%@1.0uM		
B-1357	0.18uM	84.0%@1.0uM		
B-1358	0.16uM	76.0%@1.0uM		
B-1359	0.005	84.0%@1.0uM		
B-1360	0.11	0.15uM		54%@3mpk@-4h
B-1361	0.03	0.29uM		
B-1362	0.003	0.29uM		
B-1363	0.009	0.28uM	51.0%@30pmk @-6H	53%@3mpk@-4h
B-1364	0.009	0.27uM	53.0%@30mpk@-6.0H	17%@3mpk@-4h
B-1365	0.17	88.0%@1.0uM		
B-1366	0.04	0.27uM		
B-1367	<0.1	0.22uM		
B-1368	0.031	0.33uM	44.0%@30mpk @-	
B-1369	<0.1	0.29uM		
B-1370	<0.1	0.77uM		
B-1371	0.06	83.0%@1.0uM		
B-1372	<0.1	0.41uM	48.0%@30mpk @-	
B-1373	0.016	0.17uM		
B-1374	<0.1	0.28uM		
B-1375	0.01	0.25uM		
B-1376	0.009	0.26uM	3.0%@30mpk @-6H	
B-1377	0.12	5.0uM		
B-1378	0.02	1.04uM		
B-1379	<0.1	0.092uM		
B-1380	<0.1	0.26uM		



Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1381	0.055	0.73uM		
B-1382	<0.1	0.44uM		
B-1383	0.0012	0.15uM		
B-1384	0.57	0.37uM		
B-1385	<0.1	0.11uM		
B-1386	<0.1	0.25uM		
B-1387	<0.1	0.1uM		
B-1388	0.57	1.38uM		
B-1389	0.06	0.57uM		
B-1390	<0.1	71.0%@1.0uM		
B-1391	0.016uM	82.0%@1.0uM		
B-1392	0.059uM	82.0%@1.0uM		
B-1393	3.17uM	80.0%@1.0uM		
B-1394	0.32uM	78.0%@1.0uM		
B-1395	1.48	61.0%@1.0uM		
B-1396	1.55	73.0%@1.0uM		
B-1397	0.92	85.0%@1.0uM		
B-1398	0.67	83.0%@1.0uM		
B-1399	0.14	74.0%@1.0uM		
B-1400	0.024	83.0%@1.0uM		
B-1401	0.033	75.0%@1.0uM		
B-1402	0.12	76.0%@1.0uM		
B-1403	4.54	71%@1.0uM		
B-1404	0.6	70%@1.0uM		
B-1405	0.28	70%@1.0uM		
B-1406	1.39	56.0%@1.0uM		
B-1407	0.4	71.0%@1.0uM		
B-1408	0.27	69.0%@1.0uM		
B-1409	<0.1	72.0%@1.0uM		
B-1410	<0.1	69%@1.0uM		
B-1411	<0.1	81.0%@1.0uM		
B-1412	0.097	80.0%@1.0uM		
B-1413	0.016	78.0%@1.0uM		
B-1414	0.025	83.0%@1.0uM		
B-1415	1.41	79.0%@1.0uM		
B-1416	0.14	81.0%@1.0uM		
B-1417	0.069	69.0%@1.0uM		
B-1418	1.01	82.0%@1.0uM		
B-1419	0.3	84.0%@1.0uM		
B-1420	<0.1	82.0%@1.0uM		
B-1421	0.014	75.0%@1.0uM		
B-1422	0.58	68.0%@1.0uM		
B-1423	1.58	84.0%@1.0uM		
B-1424	0.86	76.0%@1.0uM		
B-1425	0.09	83.0%@1.0uM		
B-1426	0.19	80.0%@1.0uM		
B-1427	<0.1	84.0%@1.0uM		
B-1428	<0.1	86.0%@1.0uM		
B-1429	<0.1	87.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1430	0.75uM	35.0% @1.0uM		
B-1431	0.36uM	58.0% @1.0uM		
B-1432	0.11uM	51.0% @1.0uM		
B-1433	0.26uM	21.0% @1.0uM		
B-1434	0.19uM	28.0% @1.0uM		
B-1435	1.8uM	45.0% @1.0uM		
B-1436	1.0uM	20.0% @1.0uM		
B-1437	0.3uM	23.0% @1.0uM		
B-1438	2.01uM	27.0% @1.0uM		
B-1439	1.7uM	17.0% @1.0uM		
B-1440	0.87uM	3.0% @1.0uM		
B-1441	1.95uM	66.0% @1.0uM		
B-1442	1.54uM	18.0% @1.0uM		
B-1443	0.014uM	83.0% @1.0uM		
B-1444	0.3uM	24.0% @1.0uM		
B-1445	0.43uM	27.0% @1.0uM		
B-1446	0.77uM	36.0% @1.0uM		
B-1447	0.5uM	34.0% @1.0uM		
B-1448	1.43uM	22.0% @1.0uM		
B-1449	1.61uM	50.0% @1.0uM		
B-1450	2.1uM	49.0% @1.0uM		
B-1451	2.88uM	50% @1.0uM		
B-1452	2.41uM	47.0% @1.0uM		
B-1453	2.53uM	49.0% @1.0uM		
B-1454	1.6uM	12.0% @1.0uM		
B-1455	1.21uM	8.0% @1.0uM		
B-1456	1.29uM	>1.0uM		
B-1457	0.43uM	43.0% @1.0uM		
B-1458	0.95uM	65.0% @1.0uM		
B-1459	0.67uM	46.0% @1.0uM		
B-1460	0.96uM	29.0% @1.0uM		
B-1461	0.4uM	39.0% @1.0uM		
B-1462	0.22uM	50.0% @1.0uM		
B-1463	2.34uM	26.0% @1.0uM		
B-1464	1.18uM	27.0% @1.0uM		
B-1465	3.23uM	31.0% @1.0uM		
B-1466	1.69uM	>1.0uM		
B-1467	1.22uM	1.0% @1.0uM		
B-1468	1.61uM	10.0% @1.0uM		
B-1469	0.37uM	14.0% @1.0uM		
B-1470	0.6uM	28.0% @1.0uM		
B-1471	0.85uM	25.0% @1.0uM		
B-1472	0.93uM	12.0% @1.0uM		
B-1473	1.24uM	14.0% @1.0uM		
B-1474	1.23uM	31.0% @1.0uM		
B-1475	2.1uM	24.0% @1.0uM		
B-1476	0.047uM	42.0% @1.0uM		
B-1477	2.5uM	34.0% @1.0uM		
B-1478				

	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
Example#				
B-1479				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2270	0.72uM	31%@10.0uM		
B-2271	0.93uM	38%@10.0uM		
B-2272	0.26uM	53.0%@10.0uM		
B-2273	1.92uM	39.0%@10.0uM		
B-2274	0.26uM	59.0%@10.0uM		
B-2275	2.16uM	53.0%@10.0uM		
B-2276	11.5uM	37.0%@10.0uM		
B-2277	14.9uM	44.0%@10.0uM		
B-2278	0.8uM	51.0%@10.0uM		
B-2279	0.32uM	36.0%@10.0uM		
B-2280	0.4uM	57.0%@10.0uM		
B-2281	0.81uM	60.0%@10.0uM		
B-2282	0.91uM	41.0%@10.0uM		
B-2283	0.04uM	53.0%@10.0uM		
B-2284	4.61uM	62.0%@10.0uM		
B-2285	2.29uM	49.0%@10.0uM		
B-2286	0.017uM	0.78uM	25%@30mpk@-1h	
B-2287	2.56uM	61.0%@10.0uM		
B-2288	6.51uM	46.0%@10.0uM		
B-2289	3.0uM	30.0%@10.0uM		
B-2290	2.37uM	59.0%@10.0uM		
B-2291	0.019uM	41%@10.0uM		
B-2292	8.82uM	57.0%@10.0uM		
B-2293	2.11uM	56.0%@10.0uM		
B-2294	1.68uM	50.0%@10.0uM		
B-2295	1.79uM	56.0%@10.0uM		
B-2296	17.3uM	63.0%@10.0uM		
B-2297	3.59uM	57.0%@10.0uM		
B-2298	0.29uM	4.22uM		
B-2299	1.97uM	62.0%@10.0uM		
B-2300	0.07uM	43.0%@10.0uM		
B-2301	0.18uM	44.0%@10.0uM		
B-2302	1.0uM	58.0%@1.0uM		
B-2303	0.011uM	54.0%@10.0uM		
B-2304	1.41uM	50.0%@10.0uM		
B-2305	0.54uM	60.0%@10.0uM		
B-2306	5.88uM	39.0%@10.0uM		
B-2307	2.29uM	69.0%@10.0uM		
B-2308	0.66uM	56.0%@10.0uM		
B-2309	0.29uM	47.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2310	0.12uM	1.2uM	50%@30mpk@-6h	
B-2311	7.18uM	60%@10.0uM		
B-2312	2.93uM	43.0%@10.0uM		
B-2313	42.3uM	58.0%@10.0uM		
B-2314	11.0uM	66.0%@10.0uM		
B-2315	0.49uM	36.0%@10.0uM		
B-2316	0.46uM	58.0%@10.0uM		
B-2317	1.0uM	60.0%@10.0uM		
B-2318	73.0%@10.0uM	25.0%@10.0uM		
B-2319	75.0%@10.0uM	40.0%@10.0uM		
B-2320	44.0%@10.0uM	35.0%@10.0uM		
B-2321	69.0%@10.0uM	27.0%@10.0uM		
B-2322	76.0%@10.0uM	38.0%@10.0uM		
B-2323	69.0%@10.0uM	46.0%@10.0uM		
B-2324	58.0%@10.0uM	36.0%@10.0uM		
B-2325	60.0%@10.0uM	51.0%@10.0uM		
B-2326	76.0%@10.0uM	33.0%@10.0uM		
B-2327	76.0%@10.0uM	23.0%@10.0uM		
B-2328	65.0%@10.0uM	28.0%@10.0uM		
B-2329	72.0%@10.0uM	53.0%@10.0uM		
B-2330	81.0%@10.0uM	37.0%@10.0uM		
B-2331	74.0%@10.0uM	44.0%@10.0uM		
B-2332	70.0%@10.0uM	47.0%@10.0uM		
B-2333	58.0%@10.0uM	36.0%@10.0uM		
B-2334	81.0%@10.0uM	45.0%@10.0uM		
B-2335	82.0%@10.0uM	50.0%@10.0uM		
B-2336	48.0%@10.0uM	35.0%@10.0uM		
B-2337	46.0%@10.0uM	59.0%@10.0uM		
B-2338	73.0%@10.0uM	50.0%@10.0uM		
B-2339	84.0%@10.0uM	>10.0uM		
B-2340	35.0%@10.0uM	12.0%@10.0uM		
B-2341	75.0%@10.0uM	50.0%@10.0uM		
B-2342	83.0%@10.0uM	46.0%@10.0uM		
B-2343	43.0%@10.0uM	27.0%@10.0uM		
B-2344	71.0%@10.0uM	50.0%@10.0uM		
B-2345	64.0%@10.0uM	38.0%@10.0uM		
B-2346	45.0%@10.0uM	48.0%@10.0uM		
B-2347	49.0%@10.0uM	50.0%@10.0uM		
B-2348	76.0%@10.0uM	48.0%@10.0uM		
B-2349	75.0%@10.0uM	27.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2350	38.0%@10.0uM	56.0%@10.0uM		
B-2351	77.0%@10.0uM	1.0%@10.0uM		
B-2352	37.0%@10.0uM	19.0%@10.0uM		
B-2353	38.0%@10.0uM	33.0%@10.0uM		
B-2354	65.0%@10.0uM	25.0%@10.0uM		
B-2355	84.0%@10.0uM	50.0%@10.0uM		
B-2356	77.0%@10.0uM	45.0%@10.0uM		
B-2357	47.0%@10.0uM	41.0%@10.0uM		
B-2358	17.0%@10.0uM	52.0%@10.0uM		
B-2359	76.0%@10.0uM	35.0%@10.0uM		
B-2360	45.0%@10.0uM	>10.0uM		
B-2361	19.0%@10.0uM	46.0%@10.0uM		
B-2362	60%@100.0uM	39.0%@10.0uM		
B-2363	44.0%@10.0uM	1.0%@10.0uM		
B-2364	47.0%@10.0uM	4.0%@10.0uM		
B-2365	82.0%@10.0uM	43.0%@10.0uM		
B-2366	70.0%@10.0uM	59.0%@10.0uM		
B-2367	46.0%@10.0uM	40.0%@1.0uM		
B-2368	65.0%@10.0uM	55.0%@10.0uM		
B-2369	32.0%@10.0uM	>10.0uM		
B-2370	73%@100.0uM	20.0%@10.0uM		
B-2371	54.0%@10.0uM	36.0%@10.0uM		
B-2372	55.0%@100.0uM	>10.0uM		
B-2373	50.0%@100.0uM	6%@10.0uM		
B-2374	35.0%@10.0uM	20.0%@10.0uM		
B-2375	62.0%@100.0uM	>10.0uM		
B-2376	32.0%@10.0uM	17.0%@10.0uM		
B-2377	34.0%@10.0uM	17.0%@10.0uM		
B-2378	48.0%@10.0uM	61.0%@10.0uM		
B-2379	73.0%@100.0uM	45.0%@1.0uM		
B-2380	81%@100.0uM	53.0%@10.0uM		
B-2381	68%@100.0uM	2.0%@10.0uM		
B-2382	51.0%@10.0uM	24.0%@10.0uM		
B-2383	63.0%@10.0uM	35.0%@10.0uM		
B-2384	49%@100.0uM	10.0%@10.0uM		
B-2385	79.0%@10.0uM	19.0%@10.0uM		
B-2386	38.0%@10.0uM	19.0%@10.0uM		
B-2387	50.0%@100.0uM	>10.0uM		
B-2388	42.0%@10.0uM	24.0%@10.0uM		
B-2389	39.0%@10.0uM	29.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2390	34.0%@10.0uM	27.0%@1.0uM		
B-2391	40.0%@10.0uM	59.0%@10.0uM		
B-2392	63.0%@10.0uM	46.0%@10.0uM		
B-2393	43.0%@10.0uM	>10.0uM		
B-2394	37.0%@10.0uM	22.0%@10.0uM		
B-2395	32.0%@10.0uM	28.0%@10.0uM		
B-2396	75.0%@10.0uM	>10.0uM		
B-2397	83.0%@10.0uM	22.0%@10.0uM		
B-2398	55%@100.0uM	10.0%@10.0uM		
B-2399	69.0%@10.0uM	18.0%@10.0uM		
B-2400	60.0%@10.0uM	40.0%@10.0uM		
B-2401	78.0%@10.0uM	44.0%@10.0uM		
B-2402	43.0%@10.0uM	52.0%@10.0uM		
B-2403	72%@100.0uM	52.0%@10.0uM		
B-2404	58%@100.0uM	52.0%@10.0uM		
B-2405	47%@100.0uM	>10.0uM		
B-2406	45.0%@10.0uM	24.0%@10.0uM		
B-2407	47%@100.0uM	27.0%@10.0uM		
B-2408	39.0%@10.0uM	10.0%@10.0uM		
B-2409	78.0%@10.0uM	26.0%@10.0uM		
B-2410	33.0%@10.0uM	32.0%@10.0uM		
B-2411	26%@100.0uM	13.0%@10.0uM		
B-2412	40.0%@10.0uM	31.0%@10.0uM		
B-2413	75.0%@10.0uM	37.0%@10.0uM		
B-2414	86.0%@10.0uM	38.0%@10.0uM		
B-2415	94.0%@10.0uM	50.0%@10.0uM		
B-2416	85.0%@10.0uM	43.0%@1.0uM		
B-2417	83.0%@10.0uM	18.0%@10.0uM		
B-2418	88.0%@10.0uM	34.0%@10.0uM		
B-2419	86.0%@10.0uM	66.0%@10.0uM		
B-2420	70.0%@10.0uM	34.0%@10.0uM		
B-2421	89.0%210.0uM	38.0%@10.0uM		
B-2422	90.0%@10.0uM	17.0%@10.0uM		
B-2423	85.0%@10.0uM	>10.0uM		
B-2424	86.0%@10.0uM	43.0%@10.0uM		
B-2425	79.0%@10.0uM	42.0%@10.0uM		
B-2426	88.0%@10.0uM	53.0%@10.0uM		
B-2427	87.0%@10.0uM	59.0%@10.0uM		
B-2428	82.0%@10.0uM	50.0%@10.0uM		
B-2429	92.0%@10.0uM	32.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2430	90.0% @ 10.0uM	61.0% @ 10.0uM		
B-2431	85.0% @ 10.0uM	68.0% @ 10.0uM		
B-2432	86.0% @ 10.0uM	40.0% @ 10.0uM		
B-2433	94.0% @ 10.0uM	84.0% @ 10.0uM		
B-2434	92.0% @ 10.0uM	63.0% @ 10.0uM		
B-2435	84.0% @ 10.0uM	4.0% @ 10.0uM		
B-2436	80.0% @ 10.0uM	54.0% @ 10.0uM		
B-2437	82.0% @ 10.0uM	41.0% @ 10.0uM		
B-2438	75.0% @ 10.0uM	40.0% @ 10.0uM		
B-2439	81.0% @ 10.0uM	44.0% @ 10.0uM		
B-2440	77.0% @ 10.0uM	78.0% @ 10.0uM		
B-2441	86.0% @ 10.0uM	46.0% @ 10.0uM		
B-2442	86.0% @ 10.0uM	>10.0uM		
B-2443	84.0% @ 10.0uM	44.0% @ 10.0uM		
B-2444	89.0% @ 10.0uM	7.0% @ 10.0uM		
B-2445	94.0% @ 10.0uM	15.0% @ 10.0uM		
B-2446	90.0% @ 10.0uM	28.0% @ 10.0uM		
B-2447	94.0% @ 10.0uM	>10.0uM		
B-2448	75.0% @ 10.0uM	30.0% @ 10.0uM		
B-2449	86.0% @ 10.0uM	42.0% @ 10.0uM		
B-2450	87.0% @ 10.0uM	46.0% @ 1.0uM		
B-2451	87.0% @ 10.0uM	45.0% @ 10.0uM		
B-2452	89.0% @ 10.0uM	33.0% @ 10.0uM		
B-2453	91.0% @ 10.0uM	>10.0uM		
B-2454	88.0% @ 10.0uM	40.0% @ 10.0uM		
B-2455	87.0% @ 10.0uM	54.0% @ 10.0uM		
B-2456	86.0% @ 10.0uM	53.0% @ 10.0uM		
B-2457	90.0% @ 10.0uM	18.0% @ 10.0uM		
B-2458	83.0% @ 10.0uM	36.0% @ 10.0uM		
B-2459	82.0% @ 10.0uM	81.0% @ 10.0uM		
B-2460	80.0% @ 10.0uM	79.0% @ 10.0uM		
B-2461	67.0% @ 10.0uM	59.0% @ 10.0uM		



1051

Biological data from a number of compounds of Examples C-74 through C-139 are shown in the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

**"P38 alpha kinase IC50,  $\mu$ M"**

In vitro human whole blood assay data for measuring the ability of the compounds to inhibit TNF production in human whole blood stimulated with LPS are shown in the column identified as:

**"Human Whole Blood IC50,  $\mu$ M or %Inhib@conc. ( $\mu$ M)"**

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

**"Rat LPS Model % Inhibition@dose@predose time"**

wherin the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when the compound is administered.

Example#	P38 alpha kinase IC50, $\mu$ M	Human Whole Blood IC50, $\mu$ M or %Inhib@conc. ( $\mu$ M)	Rat LPS Model % Inhibition@ dose@predose time
C-74	0.037	0.56	54%@5mpk@-4h
C-75	0.045	0.4	71%@5mpk@-4h
C-76	0.07	3.24	66%@5mpk@-4h
C-77	0.071	8.2	92%@5mpk@-4h
C-78	0.068	10.5	87%@5mpk@-4h
C-79	0.045	0.52	83%@5mpk@-4h

Example#	P38 alpha kinase IC50, $\mu\text{M}$	Human Whole Blood IC50, $\mu\text{M}$ or %Inhib@conc. ( $\mu\text{M}$ )	Rat LPS Model % Inhibition@ dose@predose time
C-80	0.008	51% @ 5 $\mu\text{M}$	
C-81	0.037	40% @ 5 $\mu\text{M}$	
C-82	0.15	7.31	
C-83	0.24	1.23	25% @ 5mpk@-4h
C-84	0.048	0.88	22% @ 5mpk@-4h
C-85	0.57	>25	
C-86	0.007	0.19	66% @ 5mpk@-4h
C-87	0.027	0.34	
C-88	0.012	0.3	59% @ 5mpk@-4h
C-89	0.039	0.12	27% @ 5mpk@-4h
C-90	0.037	0.48	
C-91	0.054	2.31	63% @ 5mpk@-4h
C-92	0.024	0.28	66% @ 5mpk@-4h
C-93	0.009	0.38	50% @ 5mpk@-4h
C-94	0.02	0.27	73% @ 5mpk@-4h
C-95	0.13	3.91	32% @ 5mpk@-4h
C-96	0.077	2.1	38% @ 5mpk@-4h
C-97	0.025	3.83	21% @ 5mpk@-4h
C-98	0.016	0.64	78% @ 5mpk@-4h
C-99	0.062	0.38	36% @ 5mpk@-4h
C-100	0.027	0.27	44% @ 5mpk@-4h
C-101	0.083	3.71	52% @ 5mpk@-4h
C-102	0.29	7.56	72% @ 5mpk@-4h
C-105	0.033	0.13	46% @ 5mpk@-4h
C-106	0.026	0.44	23% @ 5mpk@-4h
C-107	0.014	0.38	11% @ 5mpk@-4h
C-108	0.02	0.73	0% @ 5mpk@-4h
C-111	0.21	6.05	39% @ 5mpk@-4h
C-112	0.54	6.36	89% @ 5mpk@-4h
C-113	0.082	2.72	77% @ 5mpk@-4h
C-114	0.11	1.73	39% @ 5mpk@-4h
C-115	0.042	10.2	39% @ 5mpk@-4h
C-116	0.429	0.50	53% @ 5mpk@-4h
C-117	3.42	7.26	71% @ 5mpk@-4h
C-118	0.298	>25	39% @ 5mpk@-4h
C-120	0.7	18.6	26% @ 5mpk@-4h
C-121	0.11	15.3	39% @ 5mpk@-4h
C-122	0.025		55% @ 5mpk@-4h
C-123	0.67	>25.0	

1053

Example#	P38 alpha kinase IC50, $\mu$ M	Human Whole Blood IC50, $\mu$ M or %Inhib@conc. ( $\mu$ M)	Rat LPS Model % Inhibition@ dose@predose time
C-124	0.17	4.56	51%@20mpk@-4h
C-125	7.22	>25.0	
C-126	0.71	>25.0	6%@20mpk@-4h
C-127	0.038	0.27	53%@5mpk@-4h
C-128	0.09	2.22	63%@5mpk@-4h
C-132	0.086	44%@ 5 $\mu$ M	
C-133	0.16	4.54	55%@5mpk@-4h
C-135	6.0		
C-136	0.032		
C-137	0.051		58%@5mpk@-4h
C-138	0.28	0.68	26%@5mpk@-4h
C-139	0.2	3.66	46%@5mpk@-4h

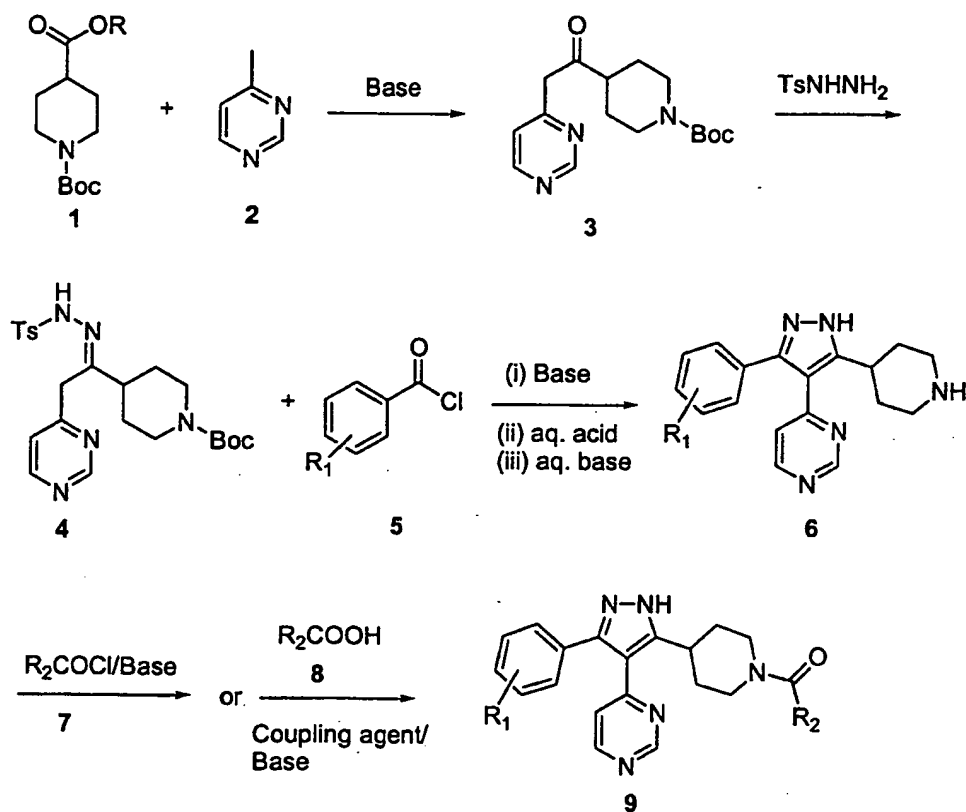
C-3015/2

1054

Additional compounds of interest can be prepared as set forth above and as described below in Scheme D-1, wherein the  $R_1$  and  $R_2$  substituents are as defined previously.

5

Scheme D-1



The synthesis begins with the treatment of 4-methylpyrimidine 2 with a base such as LiHMDS, LDA or tBuOK in an organic solvent such as THF or ether which is cooled in an ice bath (0-10 °C). To the resulting 4-methylanion is added a solution of a suitably protected (Boc is shown) ethyl ester of isonipecotic acid 1 in THF or ether. The reaction is allowed to warm to room

1055

temperature and stirred for a period of 4 hours to 20 hours at which time the desired ketone 3 is isolated after aqueous work up. Condensation of the ketone 3 with tosylhydrazide in toluene or benzene as a solvent at  
5 refluxing temperatures for a period of 1 hour to 5 hours affords the hydrazone 4. The hydrazone 4 is reacted with a suitably substituted benzoyl chloride 5, in the presence of a base such as LiHMDS or LDA or tBuOK or triethylamine at temperatures ranging from 0 °C to 70 °C. The reaction  
10 is stirred for a period of 3-6 hours. Acidic hydrolysis of the protecting groups with an aqueous acid such as HCl or H<sub>2</sub>SO<sub>4</sub> and subsequent neutralization with an aqueous base such as NaOH or KOH affords the desired pyrazole 6. Treatment of the pyrazole 6 with an acid chloride 7 in the  
15 presence of base or with an acid 8 under standard peptide coupling conditions (EDC or DCC or PyBrOP with an additive such as HOBT or HATU and base such as N-methylmorpholine or diisopropylethylamine or triethylamine) affords the desired pyrazole amide 9. In most instance the desired  
20 products can be obtained pure by direct trituration with solvents such as methanol, ethyl acetate, acetonitrile or ether and/or recrystallization from suitable solvents.

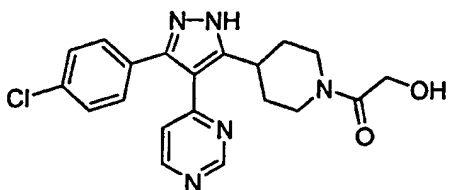
The following examples contain detailed descriptions of the methods of preparation of these additional  
25 compounds that form part of the invention. These detailed descriptions are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All compounds showed NMR spectra consistent with their assigned structures.

30

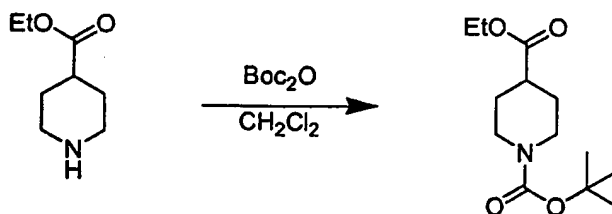
**Example D-1**

1056

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



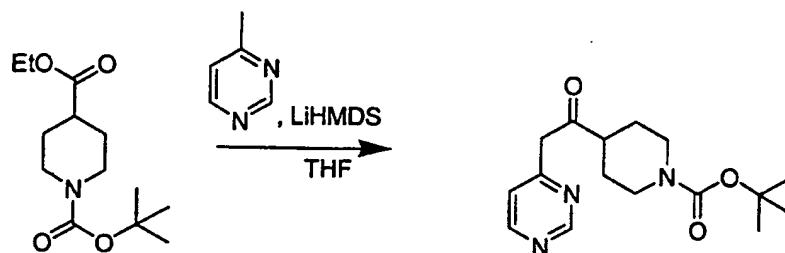
5



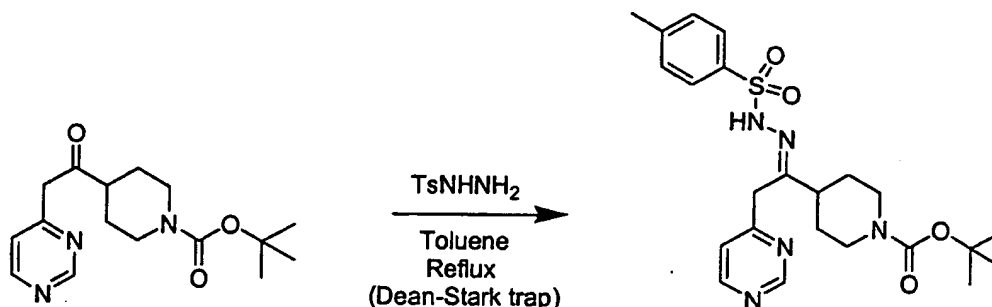
Step 1: A 5 L 4-necked round bottom flask fitted  
10 with an overhead mechanical stirrer, N<sub>2</sub> inlet and a  
thermocouple was charged with 600 g (2.75 mol) of di-tert-  
butyl-dicarbonate and 1.5 L of CH<sub>2</sub>Cl<sub>2</sub>. The solution was  
cooled to 0 °C and 428 g (2.73 mol) of ethyl isonipecotate  
was added dropwise via an addition funnel. The addition  
15 took 45 minutes and the temperature rose from 0 °C to 17.4  
°C. The reaction mixture was stirred for an additional 2  
hours at ambient temperature. The solvent was removed in  
vacuo to afford 725 g of a yellow oil (residual solvent  
remained).

20

1057



Step 2: A 3 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a N<sub>2</sub> inlet, an addition funnel and a thermocouple was charged with 1850 mL (1.85 mol) of a 1.0 M solution of LiHMDS in THF. The flask was cooled to 5 °C and 68 mL (0.74 mol) of 4-methylpyrimidine was added (neat) to the stirred solution. To this solution was added 198 g (0.77 mol) of Ethyl-N-t-butylcarbonyl isonipecotate dissolved in 160 mL of THF. The ice bath was removed and the reaction was allowed to stir for 18 hours. The reaction was quenched with 500 mL of saturated NH<sub>4</sub>Cl and was extracted with 500 mL of ethyl acetate. The organic phase was washed with 500 mL of brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo* to afford 235 g of a brown oil.



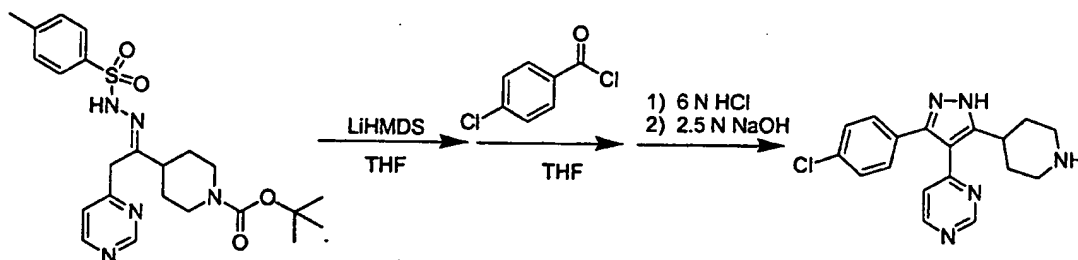
Step 3: A 2 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a Dean-Stark trap and

1058

a thermocouple was charged with 1.5 L of toluene, 226 g (0.742 mol) of N-t-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone and 138.4 g (0.743 mol) of tosyl hydrazide. The mixture was warmed to reflux. The solution was allowed to reflux for 2 hours and was cooled to ambient temperature. The reaction was allowed to stand overnight. A fine precipitate formed and was removed by filtration. The filtrate was concentrated in vacuo to afford a brown solid. The solid was suspended in 500 mL of ethyl acetate and the resulting mixture was placed in a sonication bath for 5 hours. The mixture was cooled in an ice bath and was filtered to afford 310 g of a wet solid. The solid was dried in a vacuum oven (40 °C, 5 mm) overnight to afford 248 g of the desired hydrazone (71%).

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 9.03 (d, J = 1.2 Hz, 1H), 8.72 (d, J = 5.2 Hz, 2H), 7.89 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.26 (dd, J = 5.2, 1.0 Hz, 1H), 4.03 (d, J = 12.1 Hz, 2H), 3.76 (s, 2H), 2.71 (t, J = 12.1 Hz, 2H), 2.43 (s, 3H), 2.34 (m, 1H), 1.66 (d, J = 13.5 Hz, 2H), 1.47 (s, 9H), 1.38 (m, 2H); MS (M + H): 474 (base peak).

Step 4:



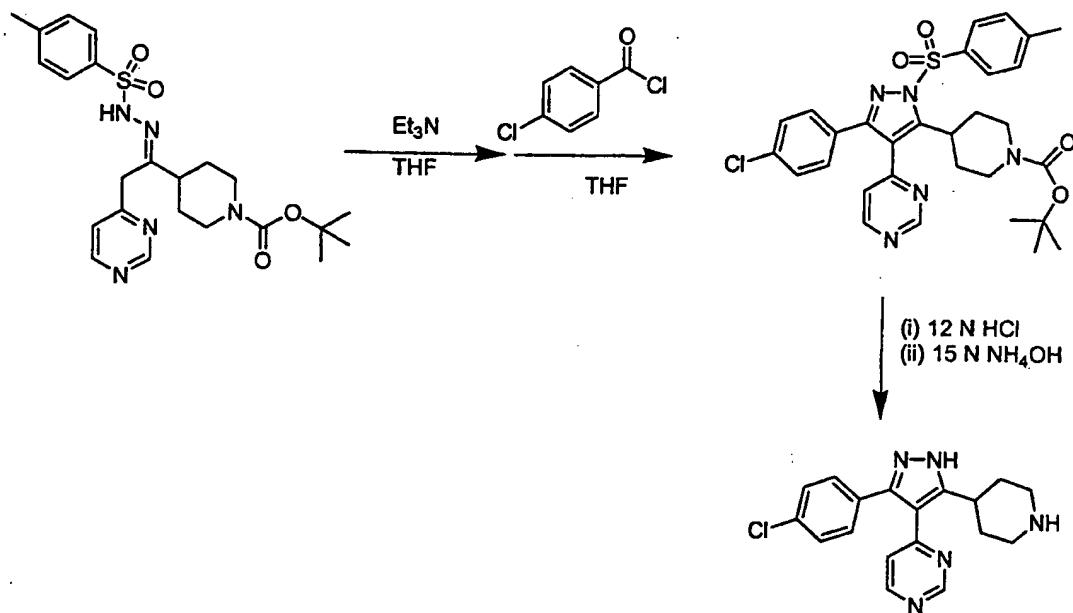


1059

Method A. A 2 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a N<sub>2</sub> inlet, an addition funnel and a thermocouple was charged with 400 mL (400 mmol) of a 1.0 M solution of LiHMDS in THF. The solution was cooled to -21.9 °C and a solution of 62 g (131 mmol) of N-t-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone p-toluenesulfonyl hydrazone in 400 mL of THF was added slowly. The temperature never exceeded -11 °C throughout the addition. The solution was re-cooled to -19.6 °C and 23.0 g (131 mmol in 250 mL of THF) of p-chlorobenzoylchloride was added slowly. The temperature never exceeded -13 °C throughout the addition. The cooling bath was removed and the reaction was allowed to warm to ambient temperature. After 3 hours the reaction was quenched with 600 mL of 3 N HCl. The reaction was warmed to reflux and was held at reflux for 2 hours. The reaction was allowed to cool to ambient temperature overnight. The reaction mixture was washed with 1.4 L of Et<sub>2</sub>O and the aqueous phase was neutralized with 1 L of 2.5 N NaOH. The aqueous phase was extracted with ethyl acetate (2 x 1000 mL). The combined organic phases were washed with brine (1 x 500 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to afford 21 g of a yellow solid. The solid was suspended in 500 mL of 2:1 Et<sub>2</sub>O/hexane. After sonication the solid was isolated by filtration to leave a wet solid. The solid was dried in a vacuum oven to afford 13.8 g of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 9.18 (s, 1H), 8.65 (d, J = 5.2, 1H), 7.44 (d, J = 8.5, 2H), 7.37 (d, J = 7.7 Hz, 2H), 7.15 (d,

1060

$J = 5.2$  Hz, 1H), 3.16 (m, 1H), 3.00 (d,  $J = 11.9$  Hz, 2H), 2.52 (m, 2H), 1.69 (m, 4H); MS (M + H): 340 (base peak).



5

**Method B:** To a solution of 200 g (423 mmol) of N-*t*-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone

10 p-toluenesulfonyl hydrazone in 800 mL THF was added 70 mL (500 mmol) of triethylamine in a 3 L three necked flask. The solution was cooled in an ice/salt/water bath to 0-5 °C. To this cold solution was added a solution of 4-chlorobenzoyl chloride (74 g, 423 mmol) in 100 mL THF

15 dropwise, maintaining the temperature below 10 °C. After the addition was complete the ice-bath was removed and replaced with a heating mantle. 4-*N*, *N*-dimethylaminopyridine (5 g, 40 mmol) was added and the reaction mixture was heated to 50 °C for 15-30 minutes.

20 The reaction mixture was filtered and the residue washed

1061

with THF (100 mL). The combined filtrates were evaporated under reduced pressure to a semisolid.

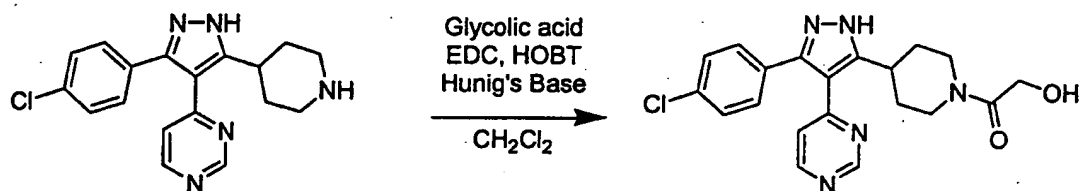
The semisolid residue was dissolved in 450 mL THF and 180 mL of 12 N HCl was added to this solution rapidly.

5 The reaction mixture was heated to 65 °C for 1.5-2 hours and transferred to a separatory funnel. The organic layer was discarded and the aqueous phase was washed twice with 200 mL of THF. The aqueous phase was transferred back to a 2 L flask and cooled to 0-10 °C in an ice bath. The pH

10 of the solution was adjusted to between ~ 9-10 by dropwise addition of 15 N ammonium hydroxide (~ 180 mL). This mixture was transferred back to a separatory funnel and extracted with warm n-butanol (3 X 150 mL). The combined n-butanol phases were evaporated under reduced pressure to

15 dryness. The residue was then stirred with methanol (200 mL), filtered and dried to obtain 129 g (90%) of the desired 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole as a off-white solid. This material was identical in all respects to the material prepared by

20 Method A.



25 Step 5: A 1 L round bottom flask was charged with 34.2 g (102 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole, 500 mL of CH<sub>2</sub>Cl<sub>2</sub> and 26.6 mL (153 mmol) of Hunig's base. To this suspension was added 16.5

1062

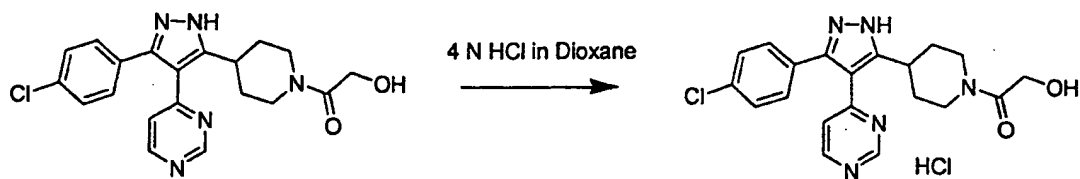
- g (122 mmol) of 1-hydroxybenzotriazole and 8.1 g (106 mmol) of glycolic acid. The addition of glycolic acid was followed by the addition of 23.7 g (122 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.
- 5 The reaction was allowed to stir at ambient temperature overnight. The reaction was concentrated in vacuo to leave an oily residue. The residue was dissolved in 400 mL of methanol and 50 mL of 2.5 N NaOH. The reaction mixture was stirred at ambient temperature for 1 hour.
- 10 The mixture was acidified to pH 5 with 2 N HCl and was extracted with CH<sub>2</sub>Cl<sub>2</sub> (6 x 200 mL). The combined organic phases were filtered through phase paper and the filtrate was concentrated in vacuo to leave a yellow residue. The residue was treated with 75 mL of acetonitrile. A
- 15 precipitate formed. The solid was filtered and washed with additional acetonitrile and Et<sub>2</sub>O to afford 31.4 g of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 9.20 (s, 1H), 8.67 (d, J = 4.8, 1H), 7.40 (m, 4H), 7.17 (d, J = 4.0, 1H), 4.53 (m, 2H), 4.13 (s, 2H), 3.77 (m, 1H), 3.05 (t, J = 12.7 Hz, 1H), 2.69 (m, 1H), 1.90 (m, 2H), 1.73 (m, 2H);
- 20 MS (M + H): 398 (base peak).

#### Example D-2

25

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride

1063



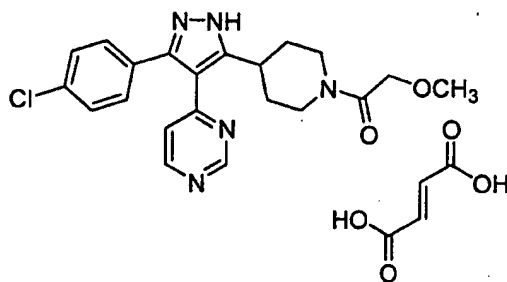
A 25 mL round bottom flask was charged with 65 mg  
 5 (0.164 mmol) of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole and 2.5 mL of dioxane. To this suspension was added 0.082 mL of 4 N HCl in dioxane. The mixture was stirred for 2 hours. The mixture was diluted with 5 mL of Et<sub>2</sub>O and filtered. The  
 10 solid was dried over solid CaSO<sub>4</sub> under vacuum for 12 h to afford 68 mg of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole hydrochloride. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 9.18(s, 1H), 8.63(d, J=5.37 Hz, 1H), 7.40(d, J=8.59 Hz, 2H), 7.33(d, J=8.59 Hz, 2H), 7.15(m,  
 15 1H), 4.40(m, 1H), 4.06(m, 2H), 3.72(m, 1H), 3.33(m, 1H), 2.97(m, 1H), 2.62(m, 1H), 1.83(m, 2H), 1.64(m, 2H); MS (M+H): 398

### Example D-3

20

N-(2-Methoxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole (fumarate salt)

1064



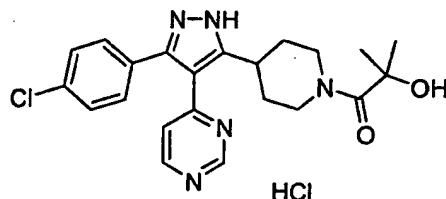
To a suspension of 250 mg (0.74 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-1, Step 3) and 180 mg (1.48 mmol) of N,N-dimethylamino pyridine in 20 mL of CH<sub>2</sub>Cl<sub>2</sub>, was added 88 mg (0.81 mmol) of 2-methoxyacetyl chloride. The reaction was stirred for 5 hours. The reaction was quenched with 20 mL of saturated NH<sub>4</sub>Cl. The mixture was extracted with n-butyl alcohol and the organic layer was washed with brine. The solvent was removed to afford 72 mg of an oil. This oil was dissolved in 1 mL of warm MeOH. This solution was combined with a warm solution of 1 equivalent of fumaric acid in warm MeOH. The solution was cooled to ambient temperature and the reaction was allowed to stir for 1 hour. The solvent was removed in vacuo and the residue was triturated with Et<sub>2</sub>O. The resulting solid was isolated by filtration to yield 56 mg of an off-white powder. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.23 (bs, 1H), 9.19 (d, J = 1.2 Hz, 1H), 8.65 (d, J = 5.1 Hz, 1H), 7.41 (m, 4H), 7.16 (dd, J = 5.4, 1.2 Hz, 1H), 4.45 (bd, J = 11.1 Hz, 1H), 4.11 (q<sub>AB</sub>, J = 39.0, 13.8 Hz, 2H), 3.86 (bd, J = 12.9 Hz, 1H), 3.32 (m, 4H), 3.04 (bt, J = 12.3 Hz, 1H), 2.63 (bt, J = 12.0 Hz, 1H), 1.77 (m, 4H); MS (M + H): 411 (base peak).

1065

## Example D-4

N-(2-Hydroxy-2-methylpropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride

5



Step 1: To a suspension of 2.05 g (6.1 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-1, Step 3) and 3.7 g (30.5 mmol) of N,N-dimethylamino pyridine in 30 mL of  $\text{CH}_2\text{Cl}_2$ , was added 1.06 mL (7.3 mmol) of 2-acetoxy-2-methylpropionyl chloride. The reaction was allowed to stir overnight at ambient temperature. The reaction was quenched with saturated  $\text{NH}_4\text{Cl}$  and water. The resulting aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were concentrated in vacuo to leave an oily solid. The residue was treated with  $\text{CH}_3\text{CN}$  and allowed to stand for 15 minutes. The resulting suspension was diluted with Et2O and was filtered to afford 2.2 g of a solid. Analysis by LC/MS indicated that the solid was a mixture of the hydroxy derivative and the acetoxy derivative. This solid was carried on to the next step without further purification.

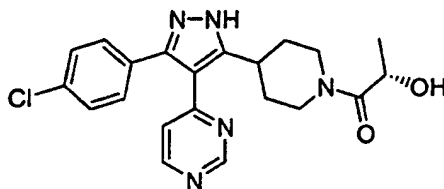
Step 2: A solution of 1 g of the solid from step 1 in 10 mL of MeOH was treated with 500 mg of solid  $\text{K}_2\text{CO}_3$ . The mixture was allowed to stir overnight at ambient

1066

temperature. The suspension was treated with water and the resulting solution was extracted with ethyl acetate. The organic phase was filtered through phase separation paper (to remove the residual water) and was concentrated in vacuo to leave an oily solid. The solid was dried under vacuum and was treated with  $\text{CH}_3\text{CN}$ . The suspension was filtered to afford 825 mg of an off-white solid. This solid was suspended in 5 mL of dioxane and 0.5 mL of 4 N HCl in dioxane was added. The suspension was stirred for 1 hour and the suspension was filtered to leave a solid. The solid was washed with  $\text{Et}_2\text{O}$  and the resulting suspension was filtered to give 900 mg of the title compound.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ) 9.23 (s, 1H), 8.69 (s, 1H), 7.45 (m, 4H), 7.19 (s, 1H), 4.8 (br m, 4H), 3.85 (m, 2H), 3.38 (m, 1H), 1.89 (m, 2H), 1.72 (m, 2H), 1.37 (s, 6H); MS (M + H): 426 (base peak).

## Example D-5

(S)-N-(2-Hydroxypropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride



By following the method of Example C-1 and substituting (S)-lactic acid for glycolic acid the title compound was prepared.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ) 13.15(s, br, 1H), 9.12(d,  $J=1.07$  Hz, 1H), 8.59(d,  $J=5.37$ Hz, 1H),



1067

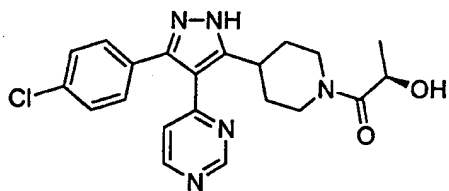
7.39(d,  $J=7.79\text{Hz}$ , 2H), 7.31(d,  $J=8.33$ , 2H), 7.10(dd,  $J=1.34$ , 5.1Hz, 1H), 4.76(m, 1H), 4.41(m, 2H), 3.99(m, 1H), 2.97(m, 1H), 2.45(m, 1H), 1.83(m, 2H), 1.64(m, 2H), 1.15(m, 3H); MS (M+H): 412 (base peak).

5

## Example D-6

(R)-N-(2-Hydroxypropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride

10



By following the method of Example C-1 and substituting (R)-lactic acid for glycolic acid the title compound was prepared.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 9.24(s, 1H), 8.52(d,  $J = 5.0\text{ Hz}$ , 1H), 7.32-7.36(m, 4H), 6.98(d,  $J = 5.3\text{ Hz}$ , 1H), 4.72(d,  $J = 10.5\text{ Hz}$ , 1H), 4.55(br, 1H), 3.88(d,  $J = 13.1\text{ Hz}$ , 1H), 3.66(br, 1H), 3.19(br, 1H), 2.82(t,  $J = 12.4\text{ Hz}$ , 1H), 2.10(br, 2H), 1.37(d,  $J = 6.2\text{ Hz}$ , 3H), 1.81-1.90(m, 2H); MS (M + H): 412 (base peak).

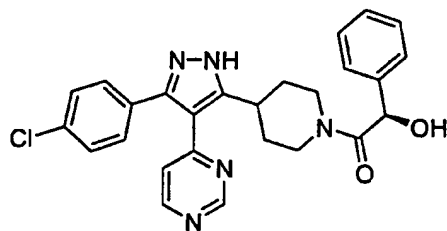
20

## Example D-7

(R)-N-(2-Hydroxy-2-phenylacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

25

1068



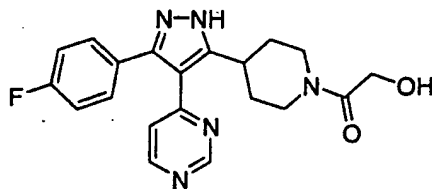
By following the method of Example C-1 and substituting (R)-phenylacetic acid for glycolic acid the  
5 title compound was prepared.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ) 9.15 (d,  $J = 0.9$  Hz, 1H), 8.63 (d,  $J = 5.4$  Hz, 1H), 7.40 (m, 9H), 7.13 (t,  $J = 6.6$  Hz, 1H), 5.43 (d,  $J = 19.5$  Hz, 1H), 4.51 (s, 1H), 4.04 (m, 1H), 3.33 (m, 4H), 2.8 (m, 2H), 1.68 (m, 3H); MS ( $M + H$ ): 474 (base peak).

10

#### Example D-8

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-  
15 fluorophenyl)pyrazole

15



By following the method of Example C-1 and substituting 4-fluorobenzoyl chloride for 4-chlorobenzoyl  
20 chloride the title compound was prepared.  $^1\text{H}$  NMR ( $\text{DMF}-d_7$ ) 13.48 (s, 1H), 9.40 (s, 1H), 8.86 (d,  $J = 5.1$  Hz, 1H), 7.71 (br, 2H), 7.42 (bd,  $J = 5.2$  Hz, 3H), 4.78 (br, 1H), 4.43 (s, 2H), 4.04 (br, 1H), 3.79 (br, 1H), 3.70 (s, 1H),

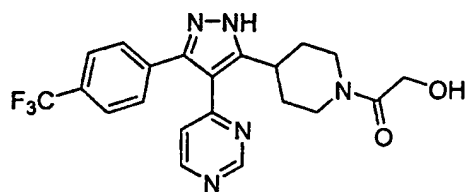
1069

3.34 (t,  $J = 12.2$  Hz, 1H), 3.0 (br, 1H), 2.21 (d,  $J = 10.9$  Hz, 2H), 2.08 (br, 1H); MS (M + H): 382 (base peak).

## Example D-9

5

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-trifluoromethylphenyl)pyrazole



10

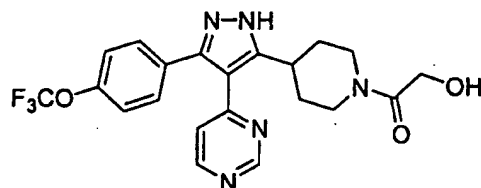
By following the method of Example C-1 and substituting 4-trifluoromethylbenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared.  $^1\text{H}$  NMR (DMF- $d_7$ ) 13.47 (s, 1H), 9.24 (s, 1H), 8.73 (d,  $J =$  4.0 Hz, 1H), 7.77 (bd,  $J = 13.3$  Hz, 4H), 7.34 (d,  $J = 4.3$  Hz, 1H), 4.61 (br, 1H), 4.26 (s, 2H), 3.87 (br, 1H), 3.52 (s, 2H), 3.17 (t,  $J = 12.0$  Hz, 1H), 2.8 (br, 1H), 2.02 (br, 2H), 1.91 (br, 1H); MS (M + H): 432 (base peak).

20

## Example D-10

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-trifluoromethoxyphenyl)pyrazole

1070

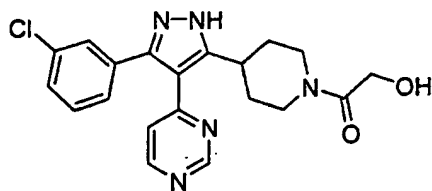


By following the method of Example C-1 and substituting 4-trifluoromethoxybenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared.

<sup>1</sup>H NMR (DMF-d<sub>7</sub>) 13.55(s, 1H), 9.40(s, 1H), 8.88(d, *J* = 4.6 Hz, 1H), 7.81(d, *J* = 7.7 Hz, 2H), 7.64(br, 2H), 7.47(d, *J* = 4.4 Hz, 1H), 4.75(br, 1H), 4.42(s, 2H), 4.04(d, *J* = 12.5 Hz, 1H), 3.69(br, 2H), 3.34(t, *J* = 12.0 Hz, 1H), 3.0(br, 1H), 2.20(d, *J* = 11.7 Hz, 2H), 2.05(br, 1H); MS (*M* + *H*): 448 (base peak).

#### Example D-11

**N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-chlorophenyl)pyrazole**



By following the method of Example C-1 and substituting 3-chlorobenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. <sup>1</sup>H NMR (DMF-d<sub>7</sub>) 13.41(s, 1H), 9.24(s, 1H), 8.73(d, *J* = 4.9 Hz, 1H), 7.56(s, 1H), 7.49(br, 2H), 7.41(br, 1H), 7.32(d, *J* = 4.2

1071

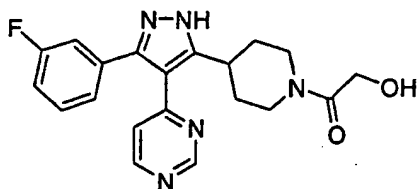
Hz, 1H), 4.60(d,  $J$  = 11.7 Hz, 1H), 4.25(s, 2H), 3.87(d,  $J$  = 12.7 Hz, 1H), 3.52(bs, 2H), 3.17(t,  $J$  = 12.1 Hz, 1H), 2.84(d,  $J$  = 12.5 Hz, 1H), 2.03(d,  $J$  = 11.9 Hz, 2H), 1.87(br, 1H); MS ( $M + H$ ): 398 (base peak).

5

**Example D-12**

**N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-fluorophenyl)pyrazole**

10



By following the method of Example C-1 and substituting 3-fluorobenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared.  $^1\text{H}$  NMR ( $\text{DMF-d}_7$ ) 13.38(s, 1H), 9.24(s, 1H), 8.72(d,  $J$  = 5.2 Hz, 1H), 7.49(dd,  $J$  = 8.0 and 6.2 Hz, 1H), 7.24-7.32(m, 4H), 4.60(d,  $J$  = 13.1 Hz, 1H), 4.25(s, 2H), 3.87(d,  $J$  = 13.3 Hz, 1H), 3.55-3.60(m, 1H), 3.52(s, 1H), 3.17(t,  $J$  = 12.2 Hz, 1H), 2.82(d,  $J$  = 12.9 Hz, 1H), 2.03(d,  $J$  = 10.9 Hz, 2H), 1.83-1.96(m, 1H); MS ( $M + H$ ): 382 (base peak).

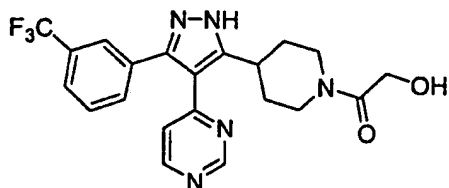
20

**Example D-13**

**N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-trifluoromethylphenyl)pyrazole**

25

1072



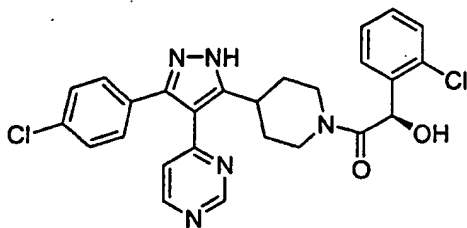
By following the method of Example C-1 and substituting 3-trifluoromethylbenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared.

<sup>1</sup>H NMR (DMF-d<sub>3</sub>) 13.76(s, 1H), 9.41(s, 1H), 8.91(d, *J* = 5.3 Hz, 1H), 8.02(s, 1H), 7.95(t, *J* = 6.5 Hz, 2H), 7.85(t, *J* = 7.5 Hz, 1H), 7.53(d, *J* = 4.6 Hz, 1H), 4.78(d, *J* = 11.9 Hz, 1H), 4.45(d, *J* = 16.3 Hz, 2H), 4.06(d, *J* = 12.5 Hz, 1H), 3.69(bs, 2H), 3.34(t, *J* = 11.3 Hz, 1H), 3.01(d, *J* = 13.1 Hz, 1H), 2.20(d, *J* = 11.1 Hz, 2H), 2.12(br, 1H); MS (M + H): 432 (base peak).

The following examples can be prepared in a manner similar to that described above for the synthesis of Examples C1-C13.

#### Example D-14

5-[4-*N*-(2-hydroxy-2-(2-chlorophenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

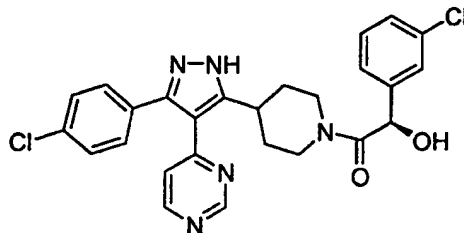


1073

## Example D-15

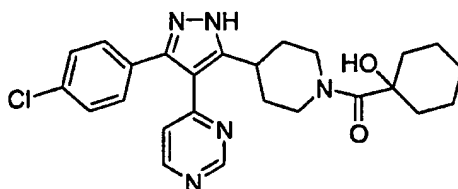
5- [4-N- (2-hydroxy-2- (3-chlorophenyl) acetyl) piperidyl] -4-  
(4-pyrimidyl) -3- (4-chlorophenyl) pyrazole

5



## Example D-16

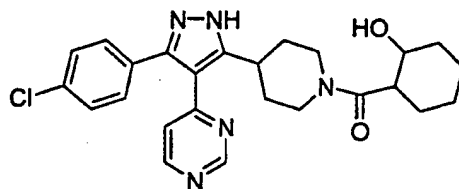
10 5- [4-N- (1-hydroxy-1-cyclohexylacetyl) piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl) pyrazole



15

## Example D-17

5- [4-N- (2-hydroxy-1-cyclohexylacetyl) piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl) pyrazole

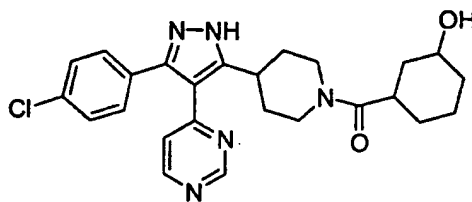


20

1074

## Example D-18

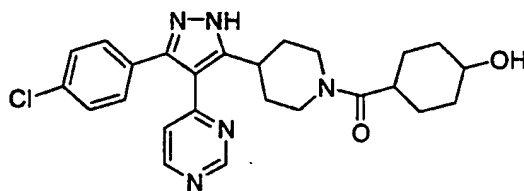
5- [4-*N*- (3-hydroxy-1-cyclohexylacetyl)piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl)pyrazole



## Example D-19

10

5- [4-*N*- (4-hydroxy-1-cyclohexylacetyl)piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl)pyrazole

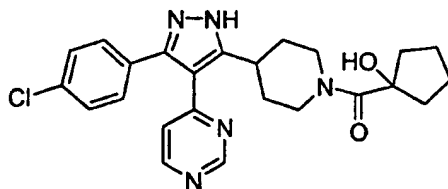


15

## Example D-20

5- [4-*N*- (1-hydroxy-1-cyclopentylacetyl)piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl)pyrazole

20

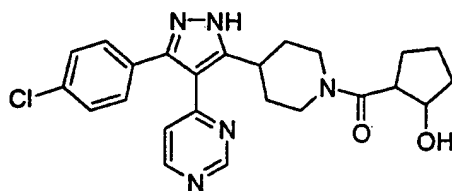




1075

## Example D-21

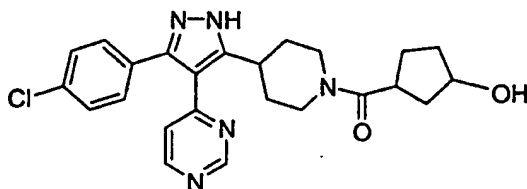
5- [4-*N*-(2-hydroxy-1-cyclopentylacetyl)piperidyl]-4-(4-  
pyrimidyl)-3-(4-chlorophenyl)pyrazole



## Example D-22

10

5- [4-*N*-(3-hydroxy-1-cyclopentylacetyl)piperidyl]-4-(4-  
pyrimidyl)-3-(4-chlorophenyl)pyrazole

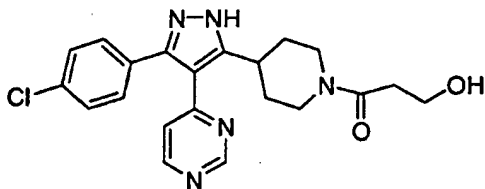


15

## Example D-23

5- [4-*N*-(3-hydroxypropionyl)piperidyl]-4-(4-pyrimidyl)-3-  
(4-chlorophenyl)pyrazole

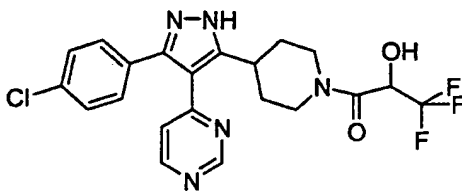
20



1076

## Example D-24

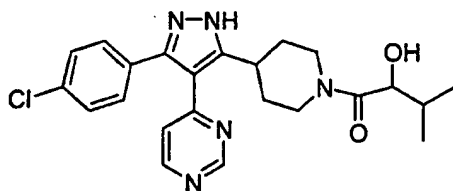
5- [4-*N*-(2-hydroxy-3,3,3-trifluoropropionyl)piperidyl] -4-  
(4-pyrimidyl) -3-(4-chlorophenyl)pyrazole



## Example D-25

10

5- [4-*N*-(2-hydroxy-3-methylbutyryl)piperidyl] -4-(4-  
pyrimidyl) -3-(4-chlorophenyl)pyrazole

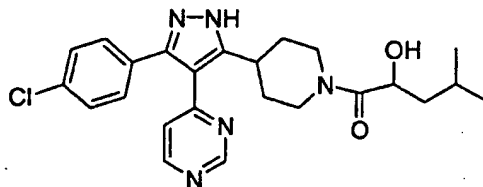


15

## Example D-26

20

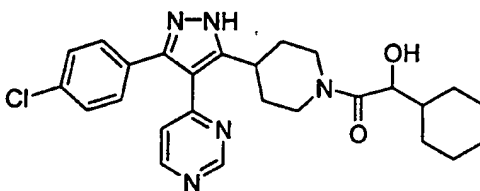
5- [4-*N*-(2-hydroxyisocaproyl)piperidyl] -4-(4-pyrimidyl) -3-  
(4-chlorophenyl)pyrazole



1077

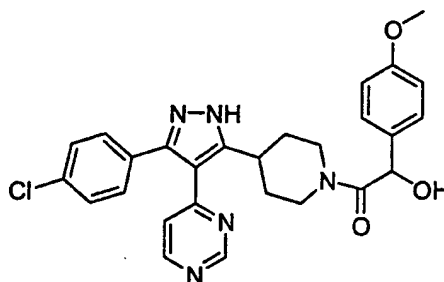
### Example D-27

5-[4-N-(2-hydroxy-2-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



### Example D-28

5-[4-N-(2-hydroxy-2-(4-methoxyphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

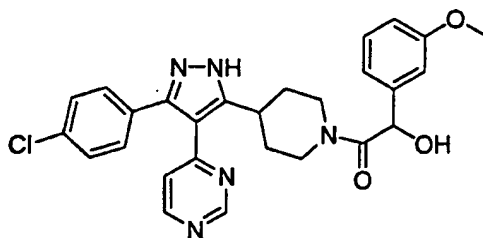


### Example D-29

5-[4-N-(2-hydroxy-2-(3-methoxyphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

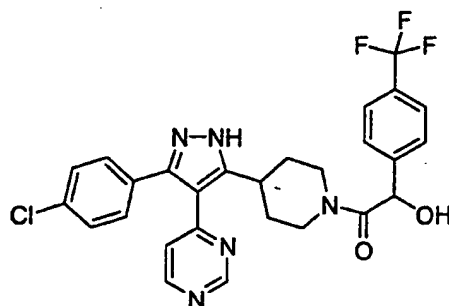
20

1078



Example D-30

5                    5-[4-N-(2-hydroxy-2-(4-trifluoromethylphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

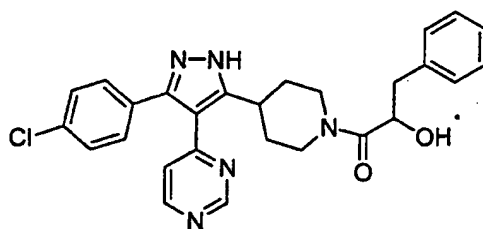


10

Example D-31

5-[4-N-(2-hydroxy-3-phenylpropionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

15

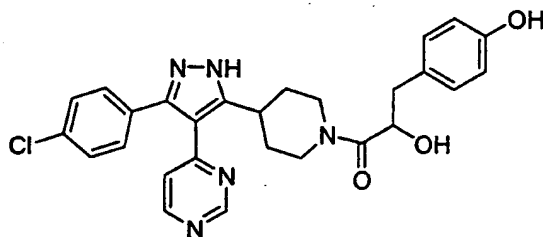


1079

## Example D-32

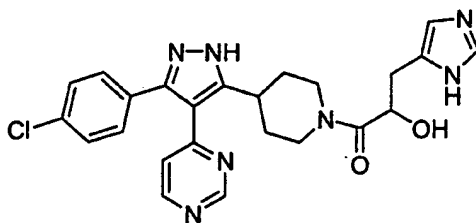
5- [4-N- (2-hydroxy-3- (4-hydroxyphenyl)propionyl)piperidyl] -  
4- (4-pyrimidyl) -3- (4-chlorophenyl)pyrazole

5



## Example D-33

10 5- [4-N- (2-hydroxy-3-imidazolpropionyl)piperidyl] -4- (4-  
pyrimidyl) -3- (4-chlorophenyl)pyrazole



15

The synthesis of 2-substituted pyrimidinyl pyrazoles is shown in Scheme 2. Reaction of 2-methylmercapto-4-methyl pyrimidine 10 with N-Boc methyl ester of isonipecotic acid (1) under basic (base selected from  
20 LiHMDS or LDA or tBuOK) conditions in an anhydrous solvent such as tetrahydrofuran or ether affords the desired ketone 11. Condensation of the ketone 11 with tosyl hydrazine under refluxing conditions in either toluene or

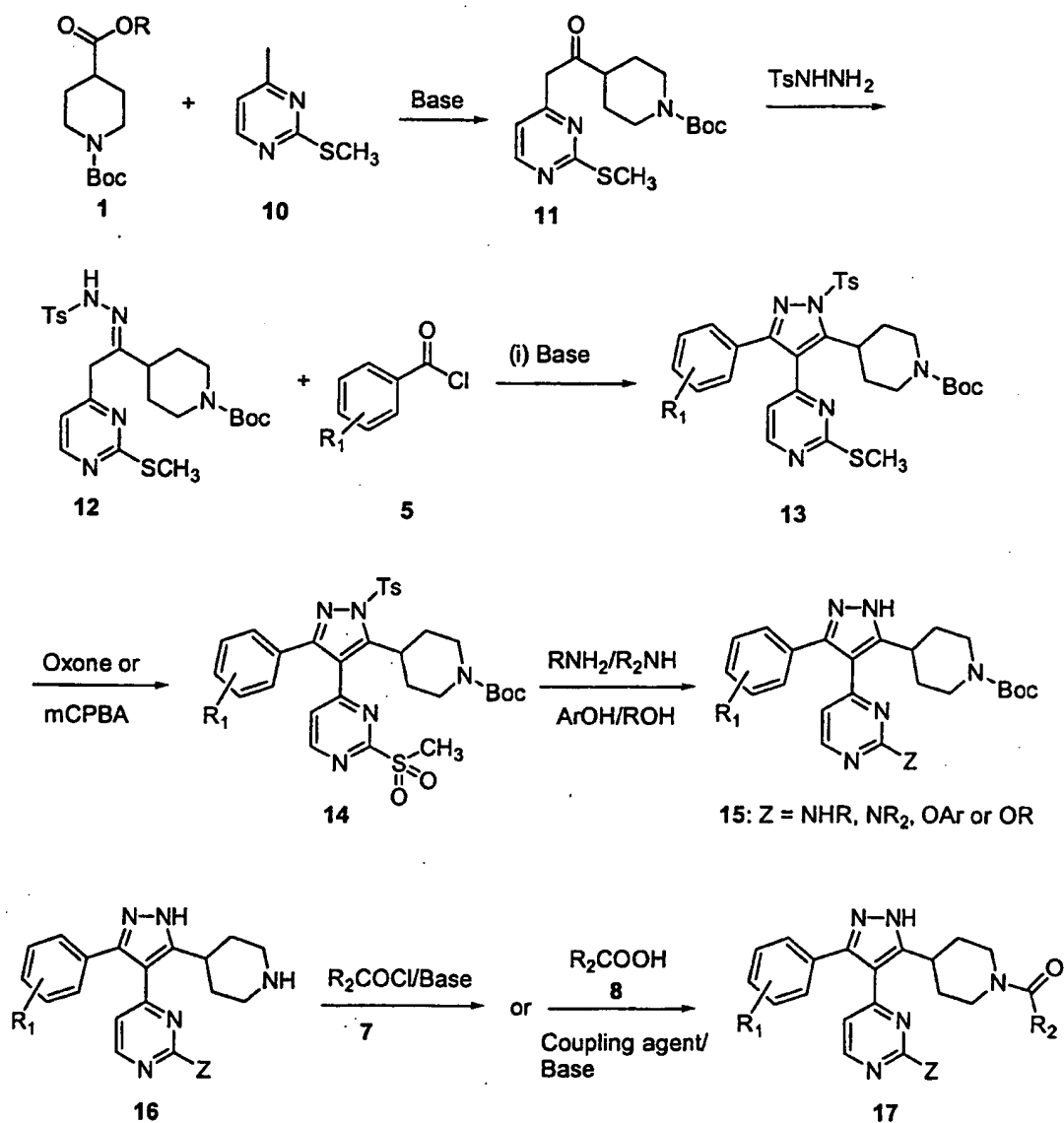
1080

benzene affords the hydrazone 12. The hydrazone 12 is deprotonated under basic (base selected from LiHMDS or LDA or tBuOK) conditions in an anhydrous solvent such as tetrahydrofuran or ether and the anion is reacted in situ  
5 with a suitably substituted benzoyl chloride 5 to afford, after mild aqueous work up, the desired and fully protected pyrazole 13. Oxidation of the 2-mercaptomethyl group present in 13 with oxidants selected from but not limited to Oxone<sup>®</sup>, H<sub>2</sub>O<sub>2</sub> or mCPBA in solvents such as  
10 dichloromethane, acetonitrile or tetrahydrofuran affords the 2-methane sulfonyl pyrazole 14. The 2-methanesulfone group in 14 is conveniently displaced with various amines, aryloxides or alkoxides in solvents such as tetrahydrofuran, dioxane, dimethylformamide or  
15 acetonitrile at temperatures ranging from 20 °C to 200 °C. Under these reaction conditions the tosyl protecting group on the pyrazole is also simultaneously deprotected. Aqueous workup affords the desired tosyl deprotected, 2-alkoxy, or 2-aryloxy or 2-amino substituted pyrazoles 15.  
20 The alkoxides or aryloxides are generated from their respective alcohols or phenols with suitable bases such as LiHMDS, NaH, LDA or tBuOK in solvents such as tetrahydrofuran, dioxane or dimethylformamide. Deprotection of the remaining N-Boc group in 15 is  
25 accomplished with trifluoroacetic acid or hydrochloric acid in solvents such as dichloromethane or dioxane to afford the pyrazole 16. Treatment of the pyrazole 16 with an acid chloride 7 in the presence of base or with an acid  
8 under standard peptide coupling conditions (EDC or DCC  
30 or PyBrOP with an additive such as HOBT or HATU and base

1081

such as N-methylmorpholine or diisopropyl ethylamine) affords the desired final products 17.

## Scheme D-2



1082

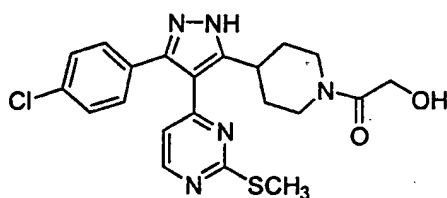
The following 2-substituted pyrimidine compounds can be prepared as set forth above, particularly in a manner similar to that outlined above in Scheme D-2.

5

**Example D-34**

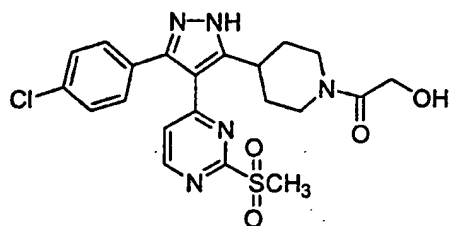
5 - [4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-thiomethyl)pyrimidyl]-3-(4-chlorophenyl)pyrazole

10

**Example D-35**

15

5 - [4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methanesulfonyl)pyrimidyl]-3-(4-chlorophenyl)pyrazole

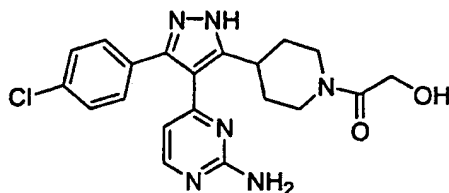
**Example D-36**

20

5 - [4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-amino)pyrimidyl]-3-(4-chlorophenyl)pyrazole

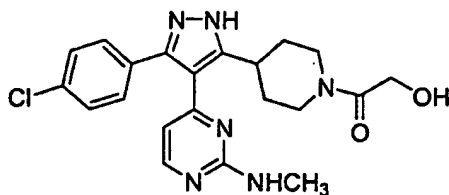


1083



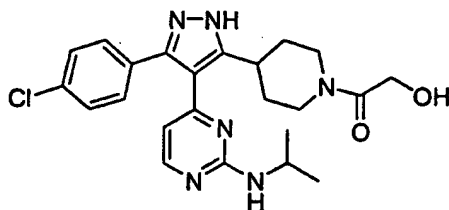
Example D-37

5            5-[4-N-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



10            Example D-38

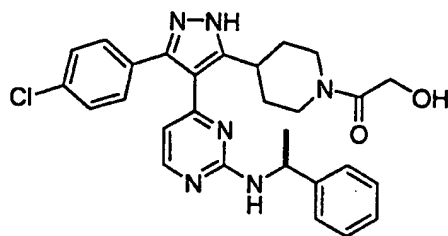
5-[4-N-(2-hydroxyacetyl)piperidyl]-4-[4-(2-isopropylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



15            Example D-39

20            5-[4-N-(2-hydroxyacetyl)piperidyl]-4-[4-(2-S-methylbenzylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole

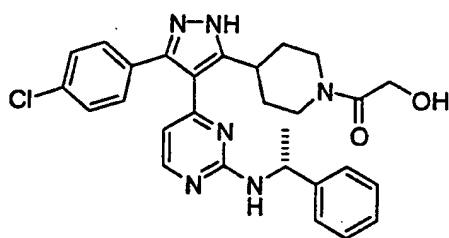
1084



Example D-40

5

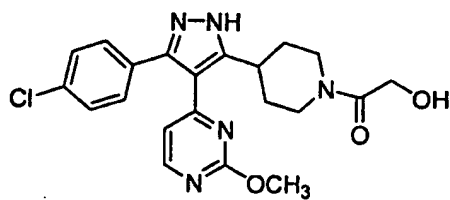
5-[4-N-(2-hydroxyacetyl)piperidyl]-4-[4-(2-R-methylbenzylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



10

Example D-41

5-[4-N-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methoxy)pyrimidyl]-3-(4-chlorophenyl)pyrazole

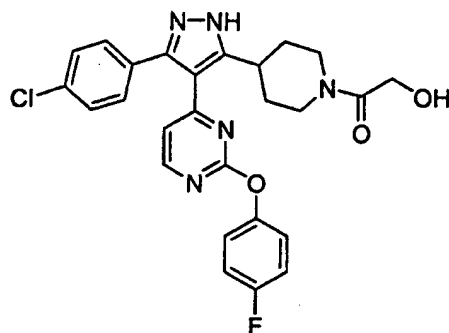


15

Example D-42

1085

5- [4-*N*-(2-hydroxyacetyl)piperidyl] -4- [4-(*p*-  
fluorophenoxy)pyrimidyl] -3-(4-chlorophenyl)pyrazole

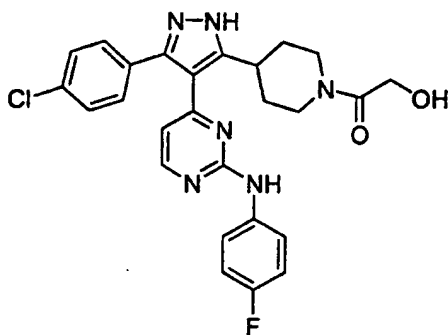


5

Example D-43

5- [4-*N*-(2-hydroxyacetyl)piperidyl] -4- [4-(*p*-  
fluoroanilino)pyrimidyl] -3-(4-chlorophenyl)pyrazole

10



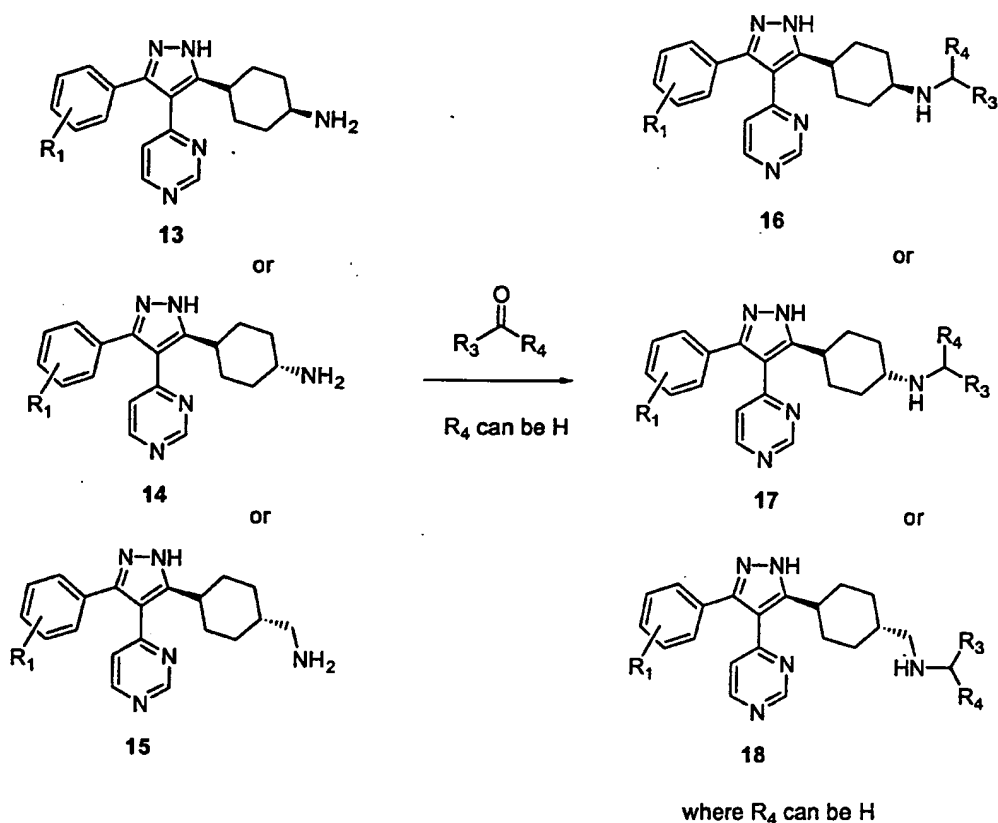
In a manner similar to that outlined above in Scheme D-1, for the synthesis of the piperidine analogs 6, the aminocyclohexane analogs are prepared by substitution of 1  
15 in Scheme D-1 with a suitably protected (Boc is shown) methyl or ethyl ester of *cis*-aminocyclohexane carboxylic acid 10 or *trans*-aminocyclohexane carboxylic acid 11 or *trans*-aminomethylcyclohexane carboxylic acid 12, which

1086

affords the cis-aminocyclohexane 13, or trans-aminocyclohexane 14 or the trans-aminomethylcyclohexane 15 respectively (Scheme 3). Suitable reductive alkylations on 13, 14 or 15 with 1-1.5 equivalents of aldehydes or ketones in the presence of a reducing agent like sodium cyanoborohydride or sodium triacetoxyborohydride in solvents such as methanol, ethanol, acetic acid, tetrahydrofuran or dichloromethane lead to the desired mono-alkylated derivatives 16, 17 or 18 respectively.

10

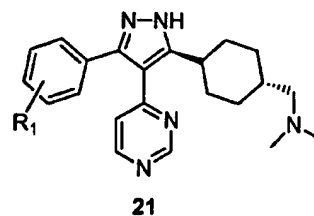
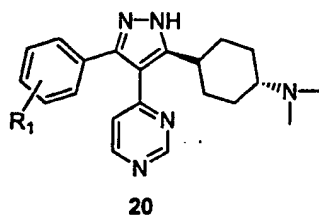
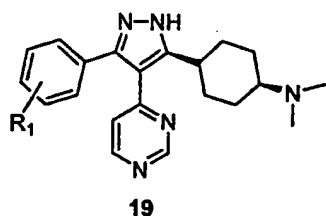
Scheme 3



The dimethyl derivatives 19, 20 or 21 can be prepared by heating a solution of the aminocyclohexanes 13, 14 or 15

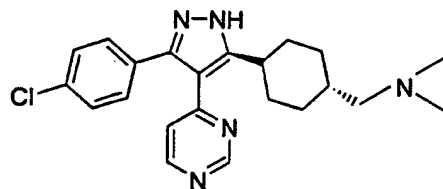
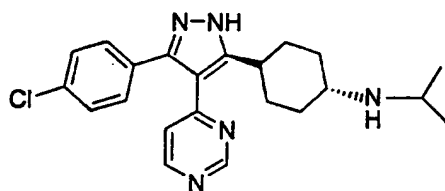
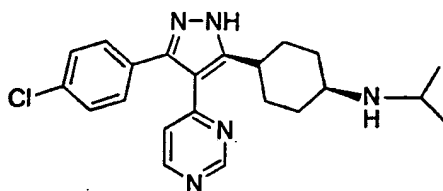
1087

respectively in a mixture of formaldehyde and formic acid at temperatures ranging from 40 °C to 110 °C.



5

An additional group of compounds of interest includes  
10 the following:



15

1088

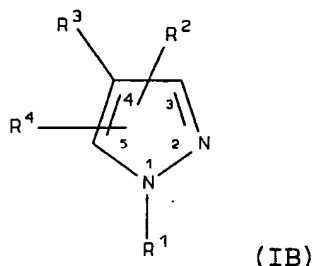
Biological data for a number of compounds are shown in the following table. In vitro p38 alpha kinase inhibitory data are shown in the column identified as "p38 alpha  $IC_{50}$  ( $\mu M$ )". In vitro human whole blood assay data for measuring the ability of the compounds to inhibit TNF production in human whole blood stimulated with LPS are shown in the column identified as: "HWB  $IC_{50}$  ( $\mu M$ )". In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF-release in the rat is shown in the column identified as: "ratLPS/%Inh@dose(mg/kg)" wherein the dose is in milligram per kilogram (mg/kg) administered by oral gavage, 4 hours before LPS challenge.

Example	p38 alpha $IC_{50}$ ( $\mu M$ )	HWB $IC_{50}$ ( $\mu M$ )	ratLPS/%Inh @1.0 (mg/kg)	ratLPS/%Inh @5.0 (mg/kg)	ratLPS/%Inh @20.0 (mg/kg)
D-1	0.17		83.0		
D-2	0.084	1.79	89.0	95.0	
D-3	0.095	0.46	69.0	88.0	91.0
D-4	0.91	1.55	42.3	83.0	99.0
D-5	0.14	4.09	65.0	78.5	83.0
D-6	0.083	1.33	82.0	96.0	100
D-7	0.44	>25.0		0	
D-8	0.18	1.3	65	85	
D-9	1.63	15.8	5	86	
D-10	3.95	14.8		80	
D-11	0.16	1.5	43	86	
D-12	0.82	7.06	71	91	
D-13	0.33	8.36	53	87	

1089

WHAT IS CLAIMED IS:

1. A compound of Formula IB:



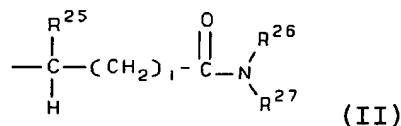
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclioxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocyclioxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocyclioxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,

1090

- 30 arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

- ```
35      i is an integer from 0 to 9;
```

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and

- 40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxy-carbonylalkylene, alkoxy-carbonyl-heterocyclyl, alkoxy-carbonyl-heterocyclyl-carbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy-carbonylarylene, aryloxy-carbonylarylene, alkylaryloxy-carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxy-carbonyl-heterocyclylarylene,



alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-\text{CHR}^{28}\text{R}^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

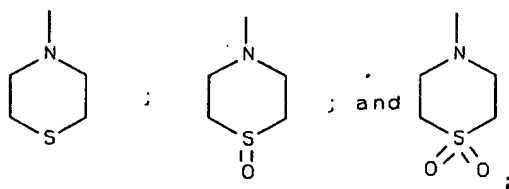
$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is piperidinyl substituted with one or more  
100 substituents selected from hydroxyalkyl, hydroxyalkenyl,  
hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene,  
alkoxyalkynylene, and hydroxyacyl, wherein said  
hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl,  
alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and  
105 hydroxyacyl substituents may be optionally substituted  
with one or more substituents selected from cycloalkyl,  
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl,  
wherein said cycloalkyl, alkyl, aryl, arylalkyl,  
haloalkyl, and heteroarylalkyl substituents may be  
110 optionally substituted with one or more substituents  
selected from alkylene, alkynylene, hydroxy, halo,  
haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; or

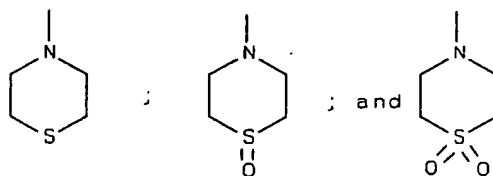
115  $R^2$  is piperidinyl substituted with one or more  
substituents selected from hydroxycycloalkyl and  
alkoxycycloalkyl, and wherein said hydroxycycloalkyl and  
alkoxycycloalkyl substituents may be optionally  
substituted with one or more substituents selected from  
120 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and  
heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl,  
arylalkyl, haloalkyl, and heteroarylalkyl substituents  
may be optionally substituted with one or more  
substituents selected from alkylene, alkynylene, hydroxy,  
125 halo, haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
130 thiazolylalkyl, thiazolylamino,

1093



wherein the R<sup>3</sup> pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 135 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more  
 substituents independently selected from hydrogen, aryl,  
 140 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,  
 arylthio, aralkoxy, wherein said aryl, alkylamino,  
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,  
 aralkoxy substituents may be optionally substituted with  
 one or more alkylene, alkenylene, hydroxy, halo,  
 145 haloalkyl, alkoxy, keto, amino, nitro, cyano,  
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
 aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 150 R<sup>4</sup> is optionally substituted with one or more substituents  
 independently selected from halo, haloalkyl, haloalkoxy,  
 alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl,  
 wherein said haloalkyl, haloalkoxy, alkoxy, cyano,  
 hydroxy, alkyl, alkenyl, and alkynyl substituents may be  
 155 optionally substituted with one or more alkylene,  
 alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,  
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,  
 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and  
 heteroaralkoxy; or

160 a pharmaceutically-acceptable salt or tautomer

thereof.

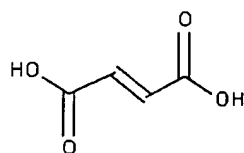
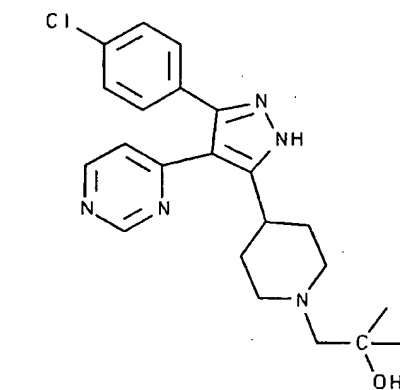
2. A compound of Claim 1 wherein:

R<sup>2</sup> is piperidinyl substituted with one or more substituents selected from hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

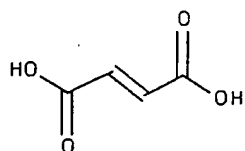
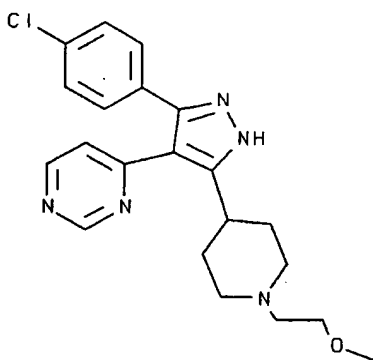
R<sup>2</sup> is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy.

1095

3. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of:

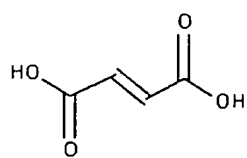
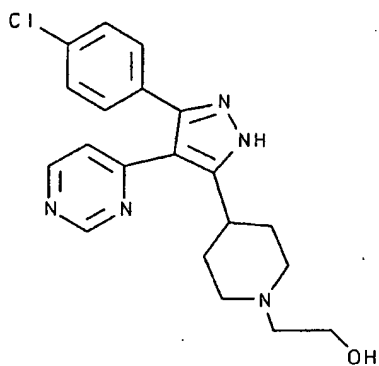


5

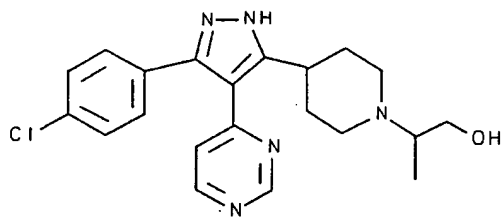


;

1096

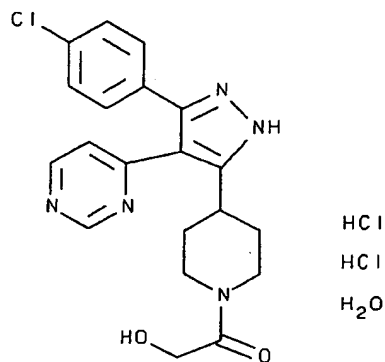


;

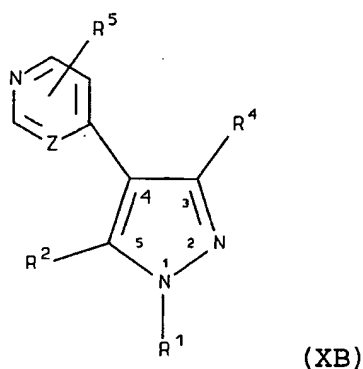


; and

1097



4. A compound of Claim 1 having Formula XB:



wherein

Z represents a carbon atom or a nitrogen atom;

R<sup>1</sup> is selected from hydrido, hydroxy, alkyl,  
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,  
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,  
 heterocyclylalkylene, haloalkyl, haloalkenyl,  
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,

alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,  
heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
alkylthioalkylene, alkenylthioalkylene,  
alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,  
alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
heterocyclylsulfonyl, alkylaminoalkylene,  
20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
heterocyclyloxycarbonylalkylene, alkoxycarbonylarylene,  
aryloxycarbonylarylene, heterocyclyloxycarbonylarylene,  
alkylcarbonylalkylene, arylcarbonylalkylene,  
25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
arylcarbonylarylene, heterocyclylcarbonylarylene,  
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
arylcarbonyloxyarylene, and  
30 heterocyclylcarbonyloxyarylene; and  
R<sup>2</sup> is piperidinyl substituted with one or more  
substituents selected from hydroxyalkyl, hydroxyalkenyl,  
alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl,  
and hydroxyalkenylcarbonyl, wherein said hydroxyalkyl,  
35 hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene,  
hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl  
substituents may be optionally substituted with one or  
more substituents selected from cycloalkyl, alkyl, aryl,  
arylalkyl, haloalkyl, and heteroarylalkyl, wherein said  
40 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and  
heteroarylalkyl substituents may be optionally  
substituted with one or more substituents selected from  
alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,  
keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,  
45 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and  
heteroaralkoxy; or



R<sup>2</sup> is piperidiny1 substituted with one or more substituents selected from hydroxycycloalkyl and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>4</sup> is selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>5</sup> represents one or more substituents independently selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer

1100

thereof.

5. A compound of Claim 4 wherein R<sup>2</sup> is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

6. A compound of Claim 4 wherein Z represents a carbon atom.

7. A compound of Claim 4 wherein Z represents a nitrogen atom.

8. A compound of Claim 4 wherein R<sup>1</sup> is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

9. A compound of Claim 4 wherein R<sup>1</sup> is hydrido.

10. A compound of Claim 4 wherein R<sup>2</sup> is piperidinyl substituted with at least one substituent selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and hydroxycycloalkylcarbonyl.

11. A compound of Claim 4 wherein R<sup>4</sup> is optionally substituted phenyl.

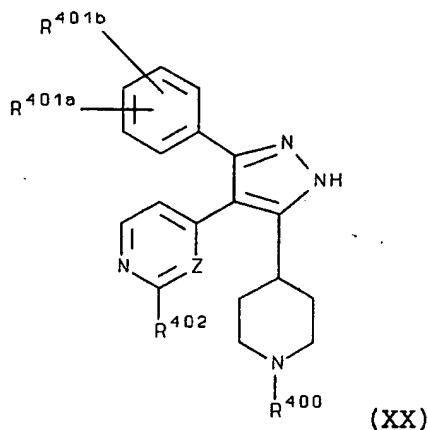
12. A compound of Claim 4 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

13. A compound of Claim 4 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

1101

14. A compound of Claim 4 wherein  $R^5$  is hydrido.

15. A compound of Claim 1 having Formula XX:



wherein:

Z represents a carbon atom or a nitrogen atom;

5  $R^{400}$  is selected from hydroxyalkyl,

hydroxyalkylcarbonyl and alkoxyalkylene, wherein said hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

20  $R^{400}$  is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and

1102

heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

$R^{401a}$  and  $R^{401b}$  are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

$R^{402}$  is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer thereof.

16. A compound of Claim 15 wherein:

$R^{400}$  is selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene, wherein said lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and

1103

lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

$R^{400}$  is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, aryloxy, heterocyclyl, and lower heteroaralkoxy; and

$R^{401a}$  and  $R^{401b}$  are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

$R^{402}$  is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said

1104

phenyl, lower alkylamino, lower alkylthio, lower  
alkyloxy, phenyloxy, phenylamino, phenylthio, and  
45 phenylalkoxy may be optionally substituted with one or  
more lower alkylene, lower alkenylene, hydroxy, halo,  
lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano,  
lower alkylsulfonyl, lower alkylsulfinyl, lower  
alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl,  
50 and lower heteroaralkoxy; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

17. A compound of Claim 15 wherein Z represents a  
carbon atom.

18. A compound of Claim 15 wherein Z represents a  
nitrogen atom.

19. A compound of Claim 15 wherein  $R^{400}$  is  
optionally substituted hydroxyalkylcarbonyl.

20. A compound of Claim 15 wherein  $R^{400}$  is  
optionally substituted hydroxycycloalkylcarbonyl.

21. A compound of Claim 15 wherein  $R^{400}$  is  
optionally substituted alkoxyalkylene.

22. A compound of Claim 15 wherein  $R^{400}$  is  
optionally substituted hydroxyalkyl.

23. A compound of Claim 15 wherein  $R^{401}$  represents  
one or more chloro, fluoro, bromo and iodo.

24. A compound of Claim 15 wherein  $R^{401}$  is meta-  
chloro or para-chloro.

25. A compound of Claim 15 wherein  $R^{402}$  is hydrido.

1105

26. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower  
hydroxyalkylcarbonyl;

5 and R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

R<sup>402</sup> is hydrido.

27. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted 2-  
hydroxyacetyl, 2-hydroxy-propionyl, 2-hydroxy-2-  
methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-  
5 hydroxypropionyl, 2-hydroxy-3-methylbutyryl, 2-  
hydroxyisocaprotyl, 2-hydroxy-3-phenylpropionyl, and 2-  
hydroxy-3-imidazolylpropionyl;

10 and R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;  
R<sup>402</sup> is hydrido.

28. A compound of Claim 27 wherein R<sup>401a</sup> is meta-  
chloro or para-chloro.

29. A compound of Claim 27 wherein R<sup>401a</sup> is para-  
chloro and R<sup>401b</sup> is hydrogen.

30. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower  
hydroxycycloalkylcarbonyl;

5 and R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

R<sup>402</sup> is hydrido.

31. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted 1-  
hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl,  
3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-  
5 cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-

1106

hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

10 R<sup>402</sup> is hydrido.

32. A compound of Claim 31 wherein R<sup>401a</sup> is meta-chloro or para-chloro.

33. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower hydroxyalkyl;

R<sup>401</sup> is selected from chloro, fluoro, bromo and iodo;

and

5 R<sup>402</sup> is hydrido.

34. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxyisopropyl;

5 R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

and

R<sup>402</sup> is hydrido.

35. A compound of Claim 34 wherein R<sup>401a</sup> is meta-chloro or para-chloro.

36. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower alkoxyalkylene;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

and

5 R<sup>402</sup> is hydrido.

37. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted methoxymethylene, methoxyethylene, methoxypropylene, methoxyisopropylene, ethoxymethylene, ethoxyethylene,



1107

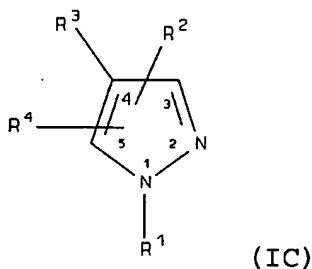
5 ethoxypropylene, and ethoxyisopropylene.

$R^{401a}$  is selected from chloro, fluoro, bromo and iodo;  
and

$R^{402}$  is hydrido.

38. A compound of Claim 37 wherein  $R^{401a}$  is meta-chloro or para-chloro.

39. A compound of Formula IC:



5 wherein

$R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene,

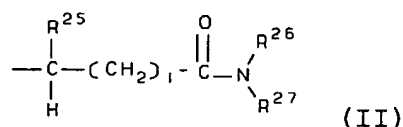
10

15

20

heterocyclyloxy carbonylalkylene, alkoxycarbonylarylene,  
 25 aryloxy carbonylarylene, heterocyclyloxy carbonylarylene,  
 alkyl carbonylalkylene, aryl carbonylalkylene,  
 heterocyclyl carbonylalkylene, alkyl carbonylarylene,  
 aryl carbonylarylene, heterocyclyl carbonylarylene,  
 alkyl carbonyloxyalkylene, aryl carbonyloxyalkylene,  
 30 heterocyclyl carbonyloxyalkylene, alkyl carbonyloxyarylene,  
 aryl carbonyloxyarylene, and  
 heterocyclyl carbonyloxyarylene; or

R<sup>1</sup> has the formula



35 wherein:

i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 40 alkyl carbonylalkylene, aryl carbonylalkylene, and  
 heterocyclyl carbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

45 R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 50 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 55 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
 alkoxycarbonylheterocyclyl carbonylalkylene, aminoalkyl,

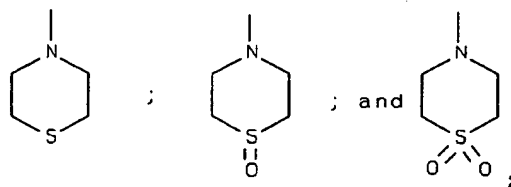
alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminoalkylene, aminocarbonylalkylene,  
arylaminoalkylene, alkylaminoalkylene,  
60 arylcarbonylalkylene, alkoxycarbonylarylene,  
aryloxycarbonylarylene, alkylaryloxycarbonylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxylarylene,  
65 heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
75 arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
80 is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
85 one or more radicals independently selected from alkyl  
and nitro; or  
R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
90 radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,

1110

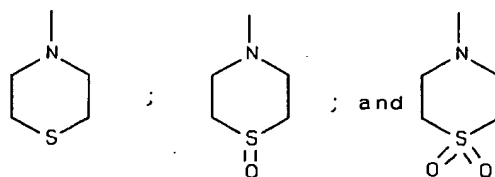
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
 95 alkoxycarbonylamino; wherein said aryl,  
 heterocyclylalkylene and aryloxyalkylene radicals may be  
 optionally substituted with one or more radicals  
 independently selected from halogen, alkyl and alkoxy;  
 and

100  $R^2$  is cyclohexyl substituted with one or more  
 substituents selected from optionally substituted  
 hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 105 thiazolylalkyl, thiazolylamino,



wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 110 thiazolylalkyl, thiazolylamino,

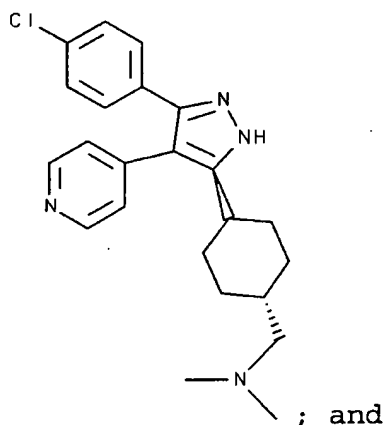


groups may be optionally substituted with one or more  
 substituents independently selected from hydrogen, aryl,  
 115 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,  
 arylthio, aralkoxy, wherein said aryl, alkylamino,  
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,  
 aralkoxy substituents may be optionally substituted with  
 one or more alkylene, alkenylene, hydroxy, halo,  
 120 haloalkyl, alkoxy, keto, amino, nitro, cyano,  
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
 aryloxy, heterocyclyl, and heteroaralkoxy; and

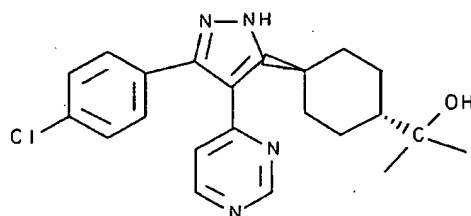
1111

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
125 R<sup>4</sup> is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl substituents may be  
130 optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or  
135 a pharmaceutically-acceptable salt or tautomer thereof.

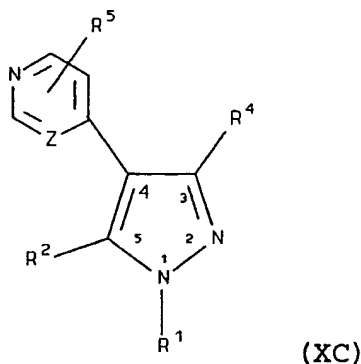
40. A compound of Claim 39 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of :



1112



41. A compound of Claim 39 having Formula XC:



wherein

Z represents a carbon atom or a nitrogen atom;

- $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino,

1113

- alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
heterocyclylsulfonyl, alkylaminoalkylene,  
20 alkylsulfonylalkylene, acyl, acyloxy carbonyl,  
alkoxycarbonylalkylene, aryloxy carbonylalkylene,  
heterocycliloxy carbonylalkylene, alkoxycarbonylarylene,  
aryloxy carbonylarylene, heterocycliloxy carbonylarylene,  
alkylcarbonylalkylene, arylcarbonylalkylene,  
25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
arylcarbonylarylene, heterocyclylcarbonylarylene,  
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
arylcarbonyloxyarylene, and  
30 heterocyclylcarbonyloxyarylene; and  
R<sup>2</sup> is cyclohexyl substituted with one or more  
substituents selected from optionally substituted  
hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and  
R<sup>4</sup> is selected from cycloalkyl, cycloalkenyl, aryl,  
35 and heterocyclyl, wherein R<sup>4</sup> is optionally substituted  
with one or more substituents independently selected from  
halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy,  
alkyl, alkenyl, and alkynyl, wherein said haloalkyl,  
haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl  
40 substituents may be optionally substituted with one or  
more alkylene, alkenylene, alkynylene, hydroxy, halo,  
haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; and  
45 R<sup>5</sup> represents one or more substituents independently  
selected from hydrogen, aryl, alkylamino, alkylthio,  
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein  
said aryl, alkylamino, alkylthio, alkyloxy, aryloxy,  
arylamino, arylthio, aralkoxy substituents may be  
50 optionally substituted with one or more alkylene,  
alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto,

1114

amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

55       a pharmaceutically-acceptable salt or tautomer thereof.

42. A compound of Claim 41 wherein R<sup>2</sup> is cyclohexyl substituted with at least one substituent attached to the 4-position carbon ring atom of the cyclohexyl ring.

43. A compound of Claim 41 wherein Z represents a carbon atom.

44. A compound of Claim 41 wherein Z represents a nitrogen atom.

45. A compound of Claim 41 wherein R<sup>1</sup> is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

46. A compound of Claim 41 wherein R<sup>1</sup> is hydrido.

47. A compound of Claim 41 wherein R<sup>2</sup> is cyclohexyl substituted with one or more substituents selected from optionally substituted lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino.

48. A compound of Claim 41 wherein R<sup>4</sup> is optionally substituted phenyl.

49. A compound of Claim 41 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

50. A compound of Claim 41 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with

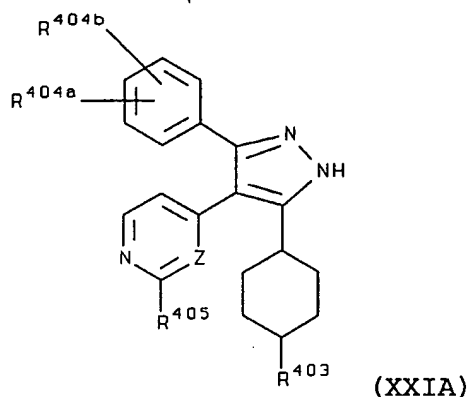


1115

one or more chloro radicals.

51. A compound of Claim 41 wherein R<sup>5</sup> is hydrido.

52. A compound of Claim 41 having Formula XXIA:



wherein:

Z represents a carbon atom or a nitrogen atom;

R<sup>403</sup> is selected from hydroxyalkyl,

5 alkylaminoalkylene and cycloalkylamino; and

R<sup>404a</sup> and R<sup>404b</sup> are independently selected from  
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,  
hydroxy, alkyl, alkenyl, and alkynyl, wherein said  
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,  
10 and alkynyl substituents may be optionally substituted  
with one or more alkylene, alkenylene, alkynylene,  
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,  
cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,  
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;  
15 and

R<sup>405</sup> is selected from hydrogen, aryl, alkylamino,  
alkylthio, alkylloxy, aryloxy, arylamino, arylthio,  
aralkoxy, wherein said aryl, alkylamino, alkylthio,  
alkylloxy, aryloxy, arylamino, arylthio, aralkoxy

1116

- 20 substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- 25 a pharmaceutically-acceptable salt or tautomer thereof.

53. A compound of Claim 52 wherein:

$R^{403}$  is selected from lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino; and

- $R^{404a}$  and  $R^{404b}$  are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
- 10

- 15  $R^{405}$  is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
- 20
- 25

a pharmaceutically-acceptable salt or tautomer thereof.

1117

54. A compound of Claim 52 wherein Z represents a carbon atom.

55. A compound of Claim 52 wherein Z represents a nitrogen atom.

56. A compound of Claim 52 wherein  $R^{403}$  is optionally substituted hydroxyalkyl.

57. A compound of Claim 52 wherein  $R^{403}$  is optionally substituted alkylaminoalkylene.

58. A compound of Claim 57 wherein  $R^{403}$  is optionally substituted dialkylaminoalkylene.

59. A compound of Claim 52 wherein  $R^{403}$  is optionally substituted cycloalkylamino.

60. A compound of Claim 52 wherein  $R^{404a}$  is selected from chloro, fluoro, bromo and iodo.

61. A compound of Claim 52 wherein  $R^{404a}$  is meta-chloro or para-chloro.

62. A compound of Claim 52 wherein  $R^{405}$  is hydrido.

63. A compound of Claim 52 wherein:

$R^{403}$  is optionally substituted lower hydroxyalkyl;

$R^{404a}$  is selected from chloro, fluoro, bromo and iodo;

5 and

$R^{405}$  is hydrido.

64. A compound of Claim 52 wherein:

$R^{403}$  is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxybutyl;

1118

- 5         $R^{404a}$  is selected from chloro, fluoro, bromo and iodo;  
and  
       $R^{405}$  is hydrido.

65. A compound of Claim 64 wherein  $R^{404a}$  is meta-chloro or para-chloro.

66. A compound of Claim 52 wherein:  
       $R^{403}$  is optionally substituted lower  
alkylaminoalkylene;  
       $R^{404a}$  is selected from chloro, fluoro, bromo and iodo;  
5    and  
       $R^{405}$  is hydrido.

67. A compound of Claim 52 wherein:  
       $R^{403}$  is selected from optionally substituted  
methylaminomethylene, methylaminoethylene,  
methylaminopropylene, ethylaminomethylene,  
5    ethylaminoethylene, ethylaminopropylene,  
propylaminomethylene, propylaminoethylene,  
propylaminopropylene, dimethylaminomethylene,  
dimethylaminoethylene, dimethylaminopropylene,  
diethylaminomethylene, diethylaminoethylene,  
10    diethylaminopropylene, dipropylaminomethylene,  
dipropylaminoethylene, and dipropylaminopropylene;  
       $R^{404a}$  is selected from chloro, fluoro, bromo and iodo;  
and  
       $R^{405}$  is hydrido.

68. A compound of Claim 67 wherein  $R^{404a}$  is meta-chloro or para-chloro.

69. A compound of Claim 52 wherein:  
       $R^{403}$  is optionally substituted cycloalkylamino;  
       $R^{404a}$  is selected from chloro, fluoro, bromo and iodo;  
and

1119

5         $R^{405}$  is hydrido.

70. A compound of Claim 52 wherein:

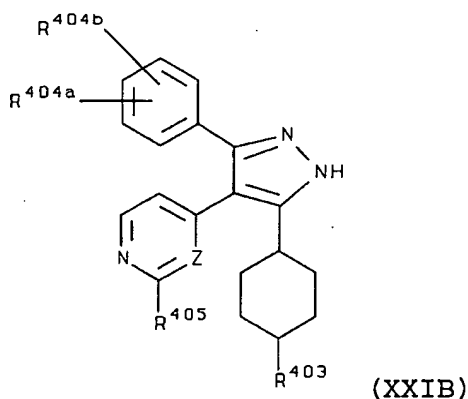
$R^{403}$  is selected from optionally substituted  
cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl;

$R^{404a}$  is selected from chloro, fluoro, bromo and iodo;

5    and

$R^{405}$  is hydrido.

71. A compound of Formula XXIB:



wherein:

Z represents a carbon atom or a nitrogen atom;

$R^{403}$  is selected from alkylamino; and

5         $R^{404a}$  and  $R^{404b}$  are independently selected from  
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,  
hydroxy, alkyl, alkenyl, and alkynyl, wherein said  
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,  
and alkynyl substituents may be optionally substituted  
10    with one or more alkylene, alkenylene, alkynylene,  
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,

1120

cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

- 15         $R^{405}$  is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or
- 20        more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- a pharmaceutically-acceptable salt or tautomer
- 25        thereof.

72. A compound of Claim 71 wherein:

$R^{403}$  is selected from lower alkylamino; and

- $R^{404a}$  and  $R^{404b}$  are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and
- 5        lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower
- 10        haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

- $R^{405}$  is selected from hydrogen, phenyl, lower
- 15        alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or
- 20        more lower alkylene, lower alkenylene, hydroxy, halo,

1121

lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

25       a pharmaceutically-acceptable salt or tautomer thereof.

73. A compound of Claim 71 wherein Z represents a carbon atom.

74. A compound of Claim 71 wherein Z represents a nitrogen atom.

75. A compound of Claim 71 wherein R<sup>403</sup> is optionally substituted dialkylamino.

76. A compound of Claim 71 wherein R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo.

77. A compound of Claim 71 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

78. A compound of Claim 71 wherein R<sup>405</sup> is hydrido.

79. A compound of Claim 71 wherein:

R<sup>403</sup> is optionally substituted lower alkylamino;

R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;

and

5       R<sup>405</sup> is hydrido.

80. A compound of Claim 71 wherein:

R<sup>403</sup> is selected from optionally substituted methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, sec-butylamino, t-butylamino, isobutylamino, dimethylamino, diethylamino, di-n-propylamino, di-isopropylamino, di-n-butylamino, di-sec-

1122

butylamino, di-t-butylamino, and di-isobutylamino;

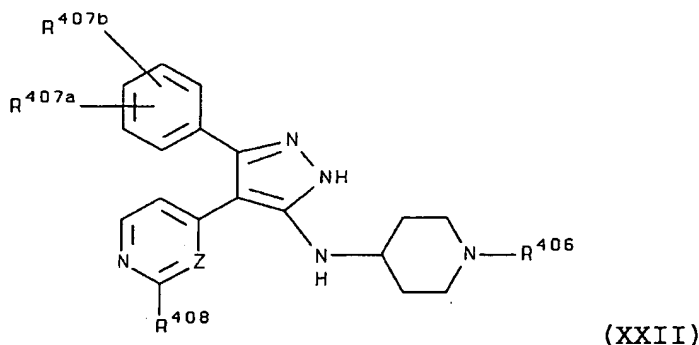
$R^{404a}$  is selected from chloro, fluoro, bromo and iodo;

and

10  $R^{405}$  is hydrido.

81. A compound of Claim 80 wherein  $R^{404a}$  is meta-chloro or para-chloro.

82. A compound Formula XXII:



wherein:

Z represents a carbon atom or a nitrogen atom;

$R^{406}$  is alkynyl; and

5  $R^{407a}$  and  $R^{407b}$  are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted  
 10 with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

15  $R^{408}$  is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio,



1123

aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or  
20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or  
a pharmaceutically-acceptable salt or tautomer  
25 thereof.

83. A compound of Claim 82 wherein:  
R<sup>406</sup> is selected from lower alkynyl; and  
R<sup>407a</sup> and R<sup>407b</sup> are independently selected from  
hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower  
alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and  
5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower  
10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and  
R<sup>408</sup> is selected from hydrogen, phenyl, lower  
15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or  
20 more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or  
25 a pharmaceutically-acceptable salt or tautomer

thereof.

84. A compound of Claim 82 wherein Z represents a carbon atom.

85. A compound of Claim 82 wherein Z represents a nitrogen atom.

86. A compound of Claim 82 wherein  $R^{407a}$  is selected from chloro, fluoro, bromo and iodo.

87. A compound of Claim 82 wherein  $R^{407a}$  is meta-chloro or para-chloro.

88. A compound of Claim 82 wherein  $R^{408}$  is hydrido.

89. A compound of Claim 82 wherein:

$R^{406}$  is optionally substituted lower alkynyl;

$R^{407a}$  is selected from chloro, fluoro, bromo and iodo;

and

5  $R^{408}$  is hydrido.

90. A compound of Claim 82 wherein:

$R^{406}$  is selected from optionally substituted ethynyl, propynyl and butynyl;

$R^{407a}$  is selected from chloro, fluoro, bromo and iodo;

5 and

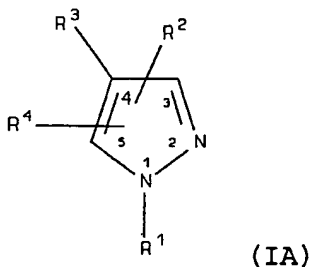
$R^{408}$  is hydrido.

91. A compound of Claim 82 wherein  $R^{406}$  is propargyl.

92. A compound of Claim 82 wherein  $R^{407a}$  is meta-chloro or para-chloro.

93. A compound of Formula IA

1125

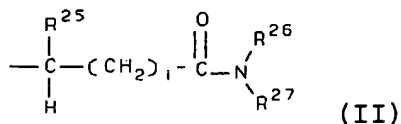


wherein

- $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula

1126



wherein:

i is an integer from 0 to 9;

- 35       $\text{R}^{25}$  is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene; and
- 40       $\text{R}^{26}$  is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and
- 45       $\text{R}^{27}$  is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclalkyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclalkyl, alkylheterocyclalkylene, alkylheterocyclalkylarylene, aralkylheterocyclalkyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclalkyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyalkylene, alkoxyalkoxyheterocyclalkyl, alkoxyalkoxyheterocyclalkylcarbonylalkylene, aminoalkyl, aminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyalkylene, aryloxyalkoxyalkylene, alkylaryloxyalkoxyalkylene, arylcarbonylalkylene, alkylaryloxyalkoxyalkylene, alkoxyalkoxyalkoxyalkylene, alkoxyalkoxyalkoxyalkylene, heterocyclalkylcarbonylalkylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,
- 50
- 55
- 60

1127

65 aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, and alkylaminosulfonylarylene;  
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,  
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
75 independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxy carbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
80 alkoxy carbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
and nitro; or

85  $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
90 alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxy carbonyl, aralkoxy carbonyl, alkylamino and  
alkoxy carbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals may be  
95 optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from mercapto,  
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,  
100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,

1128

aminoalkylcarbonylaminoalkylene,  
 alkylaminoalkylcarbonylamino, aminoalkylthio,  
 alkylaminocarbonylalkylthio,  
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,  
 105 alkenylthio, alkynylthio, carboxyalkylthio,  
 alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl,  
 alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylalkylamino,  
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
 aralkylthio, heterocyclylalkylthio, aminoalkoxy,  
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- 115 -  $(CR^{202}R^{203})_y-$ ;  
 -  $C(O)-$ ;  
 -  $C(O)-(CH_2)_y-$ ;  
 -  $C(O)-O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-C(O)-$ ;  
 120 -  $O-(CH_2)_y-C(O)-$ ;  
 -  $NR^{202}-$ ;  
 -  $NR^{202}-(CH_2)_y-$ ;  
 -  $(CH_2)_y-NR^{202}-$ ;  
 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;  
 125 -  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;  
 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;  
 130 -  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;  
 -  $O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-O-$ ;  
 -  $S-$ ; and  
 135 -  $O-$ ;  
 or  $R^{200}$  represents a bond;

1129

$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido, alkyl, aryl and aralkyl; and

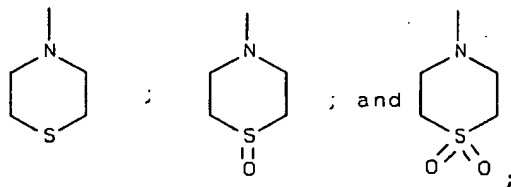
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene, and  $R^{205}$  is aryl; or

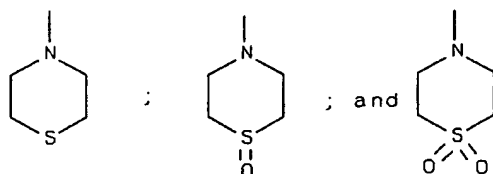
$R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl, aryl and aralkyl; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1130



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocycliloxy carbonyl, alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl) amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

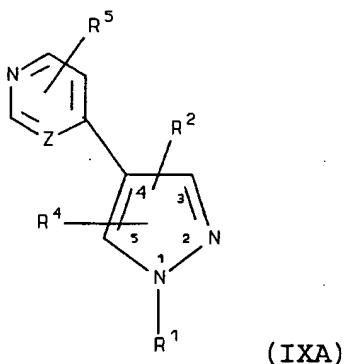
200



1131

- alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 210 provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
 ring containing a 2-hydroxy substituent and when  $R^1$  is  
 hydrido; and  
 further provided  $R^2$  is selected from  $-R^{200}-$   
 heterocyclyl- $R^{201}$ ,  $-R^{200}$ -aryl- $R^{201}$ , or  $-R^{200}$ -unsubstituted  
 215 cycloalkyl- $R^{201}$  when  $R^4$  is hydrido; and  
 further provided that  $R^4$  is not methylsulfonylphenyl  
 or aminosulfonylphenyl; and  
 further provided that  $R^1$  is not methylsulfonylphenyl;  
 or  
 220 a pharmaceutically-acceptable salt or tautomer  
 thereof.

94. A compound of Formula IXA:



wherein

Z represents a carbon atom or a nitrogen atom; and

5  $R^1$  is selected from hydrido, lower alkyl, lower

1132

hydroxyalkyl, lower alkynyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and

$R^2$  is lower hydroxyalkylamino; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$  or  $R^{200}$ -cycloalkyl- $R^{201}$

10 wherein:

$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y$ -;

- $NR^{202}$ -;

- $NR^{202}-(CH_2)_y$ -;

15 - $(CH_2)_y-NR^{202}$ -;

-O- $(CH_2)_y$ -;

- $(CH_2)_y$ -O-;

-S-;

-O-;

20 or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, lower hydroxyalkyl, lower cycloalkyl, lower hydroxyalkylcarbonyl, lower cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, lower alkoxyalkylene, lower alkoxyarylene, lower carboxyalkylcarbonyl, lower alkoxyalkylcarbonyl, lower heterocyclylalkylcarbonyl, lower alkylsulfonylalkylene, amino, lower aminoalkyl, lower aralkylamino, lower alkylaminoalkylene, aminocarbonyl, lower alkylcarbonylamino, lower alkylcarbonylaminoalkylene, lower alkylaminoalkylcarbonyl, lower alkylaminoalkylcarbonylamino, lower aminoalkylcarbonylaminoalkyl, lower alkoxycarbonylamino, lower alkoxyalkylcarbonylamino, lower alkoxycarbonylaminoalkylene, lower alkylimidocarbonyl, amidino, lower alkylamidino, lower aralkylamidino, guanidino, lower guanidinoalkylene, and lower alkylsulfonylamino; and

40  $R^{202}$  and  $R^{203}$  are independently selected from hydrido, lower alkyl, aryl and lower aralkyl; and

y is 0, 1, 2 or 3; and

1133

R<sup>4</sup> is selected from aryl selected from phenyl, biphenyl, naphthyl, wherein said aryl is optionally substituted at a substitutable position with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, and hydroxy; and

R<sup>5</sup> is selected from hydrido, halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxycarbonyl, lower alkylamino, lower hydroxyalkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower hydroxycycloalkylamino, lower alkoxycarbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is lower alkylcarbonyl or amino, and R<sup>63</sup> is lower alkyl or lower phenylalkyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

95. A compound of Claim 94 wherein R<sup>2</sup> is R<sup>200</sup>-heterocyclyl-R<sup>201</sup>.

96. A compound of Claim 94 wherein R<sup>2</sup> is R<sup>200</sup>-cycloalkyl-R<sup>201</sup>.

97. A compound of Claim 94 wherein:

R<sup>1</sup> is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperidinyl-R<sup>201</sup>, R<sup>200</sup>-piperazinyl-R<sup>201</sup>, or R<sup>200</sup>-cyclohexyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

1134

- (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

-NR<sup>202</sup>-;

-S-;

10 -O-;

or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-  
15 1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl,  
20 cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,  
35 methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminoethylene,  
40 ethylcarbonylaminoethylene, aminomethylcarbonylaminoethylene, methoxycarbonylamino, ethoxycarbonylamino,

methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
45 methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
50 methylsulfonylamino; and  
R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
55 substituted with one or more radicals independently  
selected from methylthio, fluoro, chloro, bromo, iodo,  
methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy,  
trifluoromethyl, nitro, dimethylamino, and hydroxy; and  
R<sup>5</sup> is selected from hydrido, fluoro, chloro, bromo,  
60 iodo, hydroxy, methyl, ethyl, propyl, benzyl,  
fluorophenylethyl, fluorophenylethenyl,  
fluorophenylpyrazolyl, cyano, carboxy, methoxy,  
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
dimethylamino, 2-methylbutylamino, ethylamino,  
65 dimethylaminoethylamino, hydroxyethylamino,  
hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
70 hydroxy)ethylamino, piperidinylamino,  
pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
75 fluorophenylethylamino, methylaminoethylamino,  
dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,

1136

80 dimethylaminopentylamino, ethylaminoethylamino,  
 diethylaminoethylamino, ethylaminopropylamino,  
 diethylaminopropylamino, ethylaminobutylamino,  
 diethylaminobutylamino, ethylaminopentylamino,  
 methylaminocarbonyl, methylcarbonyl, ethylcarbonyl,  
 hydrazinyl, and 1-methylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$   
 85 is methylcarbonyl or amino, and  $R^{63}$  is methyl or benzyl;  
 or

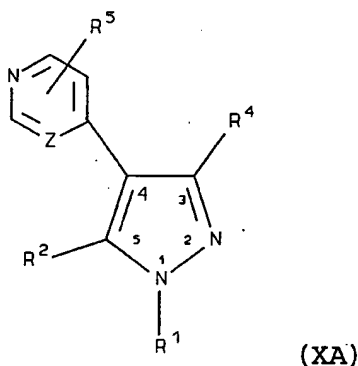
a pharmaceutically-acceptable salt or tautomer thereof.

98. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$ .

99. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -pyrazinyl- $R^{201}$ .

100. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -cyclohexyl- $R^{201}$ .

101. A compound of Claim 94 having the Formula XA:



wherein:

Z represents a carbon atom or a nitrogen atom; and  
 $R^1$  is selected from hydrido, methyl, ethyl,

1137

hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

$-(CR^{202}R^{203})_y-$ ;

10  $-NR^{202}-$ ;

$-S-$ ;

$-O-$ ;

or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from

15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,

20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,

25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,

30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,

35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N,N-dipropylamino, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene,

40 methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino,

- methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
45 aminomethylcarbonylaminocarbonylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
50 ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and  
55  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
 $R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
60 selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
 $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
65 methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
70 imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
75 phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,  
dimethylaminoethylamino, methylaminopropylamino,



1139

dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
80 dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;

85 or

a pharmaceutically-acceptable salt or tautomer thereof.

102. A compound of Claim 101 wherein:

R<sup>1</sup> is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperidinyl-R<sup>201</sup> wherein:

5 R<sup>200</sup> is selected from:

methylene;

-NR<sup>202</sup>-;

-S-;

-O-;

10 or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, methoxymethyl, methoxyethyl,  
15 methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,  
propoxypropyl, methoxyphenyl, ethoxyphenyl,  
propoxyphenyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, carboxymethylcarbonyl,  
carboxyethylcarbonyl, methoxymethylcarbonyl,  
20 methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
25 propoxyphenylcarbonyl, methylsulfonylmethylene, amino,

1140

aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethylene, aminocarbonyl, methoxycarbonylamino, ethoxycarbonylamino, or methylsulfonylamino; and

30         $R^{202}$  is selected from hydrido, methyl, ethyl, phenyl and benzyl; and

$R^4$  is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, ethyl, methoxy and  
35        ethoxy; and

$R^5$  is selected from hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino,  
40        hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino,  
45        methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino,  
50        methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl,  
55        methylcarbonyl, and ethylcarbonyl; or

      a pharmaceutically-acceptable salt or tautomer thereof.

103. A compound of Claim 101 wherein:

$R^1$  is hydrido; and

$R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$  wherein:

1141

R<sup>200</sup> is selected from:

5 methylene;

-NR<sup>202</sup>-;

-S-;

-O-;

or R<sup>200</sup> represents a bond;

10 R<sup>201</sup> represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, methoxymethyl, methoxyethyl,  
methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,  
propoxypropyl, methoxyphenyl, ethoxyphenyl,  
15 propoxyphenyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, carboxymethylcarbonyl,  
carboxyethylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, ethoxymethylcarbonyl,  
ethoxyethylcarbonyl, methoxyphenylcarbonyl,  
20 ethoxyphenylcarbonyl, amino, aminomethyl, aminoethyl,  
aminopropyl, N-benzylamino, methylaminomethylene,  
aminocarbonyl, methoxycarbonylamino, and  
ethoxycarbonylamino; and

25 R<sup>202</sup> is selected from hydrido, methyl phenyl and  
benzyl; and

R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, and methoxy; and

R<sup>5</sup> is selected from hydrido, methylamino,  
30 dimethylamino, 2-methylbutylamino, ethylamino,  
dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
35 ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, dimethylaminoethylamino,  
dimethylaminopropylamino, dimethylaminobutylamino,  
dimethylaminopentylamino, diethylaminoethylamino,  
diethylaminopropylamino, diethylaminobutylamino, and

1142

40 diethylaminopentylamino; or  
a pharmaceutically-acceptable salt or tautomer thereof.

104. A compound of Claim 101 wherein:

$R^1$  is hydrido; and

$R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

5 methylene;

- $NR^{202}$ -;

-S-;

-O-;

or  $R^{200}$  represents a bond;

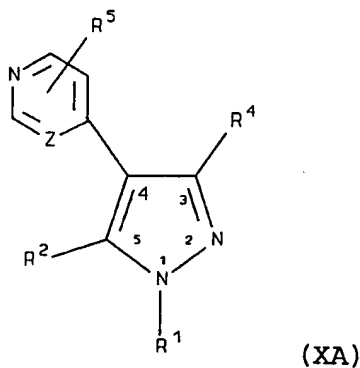
10  $R^{201}$  represents one or more radicals selected from the group consisting of methoxyethyl, methylcarbonyl, hydroxymethylcarbonyl, methoxymethylcarbonyl, and amino; and

$R^{202}$  is selected from hydrido and methyl; and

15  $R^4$  is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, and methoxy; and

$R^5$  is selected from hydrido, hydroxypropylamino, hydroxycyclohexylamino, diethylaminoethylamino; or  
20 a pharmaceutically-acceptable salt or tautomer thereof.

105. A compound of Claim 94 having the Formula XA:



1143

wherein:

Z represents a carbon atom or a nitrogen atom; and

5       R<sup>1</sup> is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperazinyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

10       -NR<sup>202</sup>-;

-S-;

-O-;

or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from

15       the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-  
1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
cyclohexyl, methoxymethylene, methoxyethylene,  
methoxypropylene, ethoxyethylene, ethoxypropylene,  
20       propoxyethylene, propoxypropylene, methoxyphenylene,  
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,  
cyclobutylcarbonyl, cyclopentylcarbonyl,  
cyclohexylcarbonyl, benzoyl, chlorobenzoyl,  
fluorobenzoyl, hydroxymethylcarbonyl,  
25       hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
30       ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
35       methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,

1144

40 methylcarbonylamino, ethylcarbonylamino,  
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
50 methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
55 y is 0, 1 or 2; and

$R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and

60  $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
65 hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
70 pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,

1145

75 dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
80 diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;  
or

a pharmaceutically-acceptable salt or tautomer  
85 thereof.

106. A compound of Claim 105 wherein:

$R^1$  is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -piperazinyl- $R^{201}$  wherein:

5  $R^{200}$  is selected from:

- $(CR^{202}R^{203})_y$ -;

- $NR^{202}$ -;

-S-;

-O-;

10 or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
15 cyclohexyl, methoxymethylene, methoxyethylene,  
ethoxyethylene, methoxyphenylene, ethoxyphenylene,  
cyclopropylcarbonyl, cyclobutylcarbonyl,  
cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl,  
chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,  
20 hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,

1146

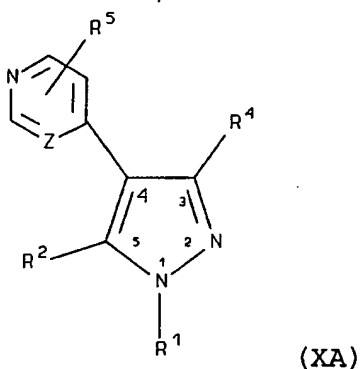
- 25 ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
30 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
methylcarbonylamino, ethylcarbonylamino,  
35 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
40 methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, and methylsulfonylamino;  
and
- 45  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
 $R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
50 selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
 $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,  
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
55 dimethylamino, ethylamino, dimethylaminoethylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
ethyl-2-hydroxy)ethylamino, aminomethyl,  
60 cyclopropylamino, amino, ethoxycarbonylamino,



1147

methoxyphenylmethylamino, phenylmethylamino,  
 fluorophenylmethylamino, fluorophenylethylamino,  
 methylaminoethylamino, dimethylaminoethylamino,  
 methylaminopropylamino, dimethylaminopropylamino,  
 65 methylaminobutylamino, dimethylaminobutylamino,  
 methylaminopentylamino, dimethylaminopentylamino,  
 ethylaminoethylamino, diethylaminoethylamino,  
 ethylaminopropylamino, diethylaminopropylamino,  
 ethylaminobutylamino, diethylaminobutylamino,  
 70 ethylaminopentylamino, methylaminocarbonyl,  
 methylcarbonyl, and ethylcarbonyl; or  
 a pharmaceutically-acceptable salt or tautomer  
 thereof.

107. A compound of Claim 94 having the Formula XA:



wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R<sup>1</sup> is selected from hydrido, methyl, ethyl,  
 hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-cyclohexyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

10 -NR<sup>202</sup>-;

-S-;

-0-;

or  $R^{200}$  represents a bond;

R<sup>201</sup> represents one or more radicals selected from

- 15 the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-  
1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
cyclohexyl, methoxymethylene, methoxyethylene,  
methoxypropylene, ethoxyethylene, ethoxypropylene,  
20 propoxyethylene, propoxypropylene, methoxyphenylene,  
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,  
cyclobutylcarbonyl, cyclopentylcarbonyl,  
cyclohexylcarbonyl, benzoyl, chlorobenzoyl,  
fluorobenzoyl, hydroxymethylcarbonyl,  
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
30 ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
methylcarbonylamino, ethylcarbonylamino,  
40 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,

ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
50 methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
55  $y$  is 0, 1 or 2; and

$R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and

60  $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
65 hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
70 pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,  
75 dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
80 diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;  
or

1150

a pharmaceutically-acceptable salt or tautomer  
85 thereof.

108. A compound of Claim 107 wherein:

$R^1$  is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -cyclohexyl- $R^{201}$  wherein:

5  $R^{200}$  is selected from:

$-(CR^{202}R^{203})_y-$ ;

$-NR^{202}-$ ;

$-S-$ ;

$-O-$ ;

10 or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
15 cyclohexyl, methoxymethylene, methoxyethylene,  
methoxypropylene, ethoxyethylene, ethoxypropylene,  
propoxyethylene, propoxypropylene, methoxyphenylene,  
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,  
cyclobutylcarbonyl, cyclopentylcarbonyl,  
20 cyclohexylcarbonyl, benzoyl, chlorobenzoyl,  
fluorobenzoyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
25 methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
30 propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,

1151

methyaminomethylene, ethylaminomethylene,  
35 methyaminomethylene, ethylaminomethylene, aminocarbonyl,  
methylcarbonylamino, ethylcarbonylamino,  
methyaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
40 aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene, and  
45 ethoxycarbonylaminomethylene; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, phenyl and benzyl; and

y is 0, 1 or 2; and

$R^4$  is phenyl, wherein said phenyl is optionally  
50 substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and

$R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,  
55 methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
dimethylamino, ethylamino, dimethylaminoethylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
60 ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, ethoxycarbonylamino,  
methoxyphenylmethylamino, phenylmethylamino,  
fluorophenylmethylamino, fluorophenylethylamino,  
methylaminoethylamino, dimethylaminoethylamino,  
65 methylaminopropylamino, dimethylaminopropylamino,  
methylaminobutylamino, dimethylaminobutylamino,  
methylaminopentylamino, dimethylaminopentylamino,  
ethylaminoethylamino, diethylaminoethylamino,  
ethylaminopropylamino, diethylaminopropylamino,

1152

- 70 ethylaminobutylamino, diethylaminobutylamino,  
ethylaminopentylamino, methylaminocarbonyl,  
methylcarbonyl, and ethylcarbonyl; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

109. A compound of Claim 107 wherein:

$R^1$  is hydrido; and

$R^2$  is  $R^{200}$ -cyclohexyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

5 methylene;

- $NR^{202}$ -;

-S-;

-O-;

or  $R^{200}$  represents a bond;

- 10  $R^{201}$  represents one or more radicals selected from  
the group consisting of amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
15 methylcarbonylamino, ethylcarbonylamino,  
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylamino, aminocarbonylmethylene,  
20 methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene, and  
ethoxycarbonylaminomethylene; and

- 25  $R^{202}$  is selected from hydrido, methyl, phenyl and  
benzyl; and

$R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, and methoxy; and

- 30  $R^5$  is selected from hydrido, methylamino,

1153

dimethylamino, 2-methylbutylamino, ethylamino,  
dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
35 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, dimethylaminoethylamino,  
dimethylaminopropylamino, dimethylaminobutylamino,  
dimethylaminopentylamino, diethylaminoethylamino,  
40 diethylaminopropylamino, diethylaminobutylamino, and  
diethylaminopentylamino; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

110. A compound of Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperidinyl or piperazinyl moiety with at  
least one substituent attached to the distal nitrogen  
heteroatom or to a carbon ring atom adjacent to the  
5 distal nitrogen heteroatom of the piperidine or  
piperazine ring.

111. A compound Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperidinyl moiety with at least one  
substituent attached to the distal nitrogen heteroatom or  
to a carbon ring atom adjacent to the distal nitrogen  
5 heteroatom of the piperidine ring.

112. A compound of Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperazinyl moiety with at least one  
substituent attached to the distal nitrogen heteroatom or  
to a carbon ring atom adjacent to the distal nitrogen  
5 heteroatom of the piperazine ring.

113. A compound of Claim 94 wherein Z represents a  
carbon atom.

1154

114. A compound of Claim 94 wherein Z represents a nitrogen atom.

115. A compound of Claim 94 wherein R<sup>1</sup> is hydrido.

116. A compound of Claim 94 wherein R<sup>200</sup> represents a bond.

117. A compound of Claim 94 wherein R<sup>201</sup> represents one or more radicals selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

118. A compound of Claim 94 wherein R<sup>201</sup> represents one or more radicals selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, 5 hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethylene, ethylaminomethylene, methylaminoethylene, and ethylaminoethylene.

119. A compound of Claim 94 wherein R<sup>4</sup> is optionally substituted phenyl.

120. A compound of Claim 94 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

121. A compound of Claim 94 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

122. A compound of Claim 94 wherein R<sup>5</sup> is hydrido.



1155

123. A compound of Claim 94 wherein:

R<sup>1</sup> is hydrido;

R<sup>200</sup> represents a bond;

5 R<sup>201</sup> represents one or more radicals selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from halo; and

10 R<sup>5</sup> is hydrido.

124. A compound of Claim 94 wherein:

R<sup>1</sup> is hydrido;

R<sup>200</sup> represents a bond;

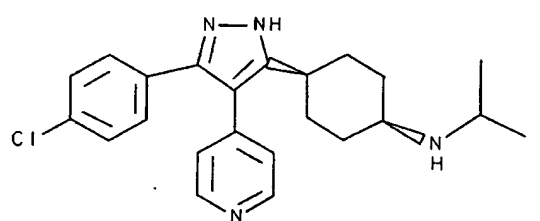
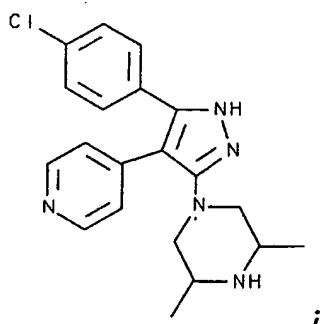
5 R<sup>201</sup> represents one or more radicals selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethylene, ethylaminomethylene, 10 methylaminoethylene, and ethylaminoethylene;

R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo; and

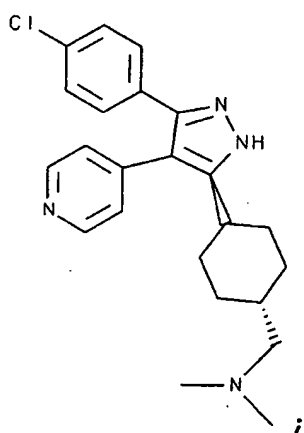
15 R<sup>5</sup> is hydrido.

125. A compound selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of:

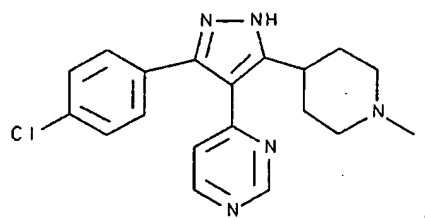
1156



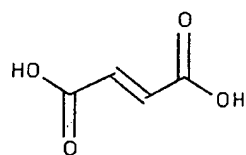
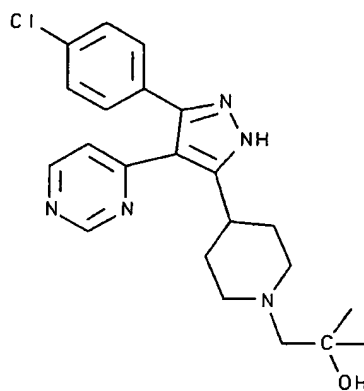
5



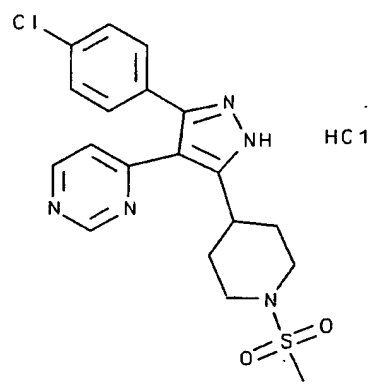
1157



;

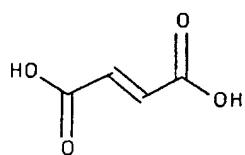
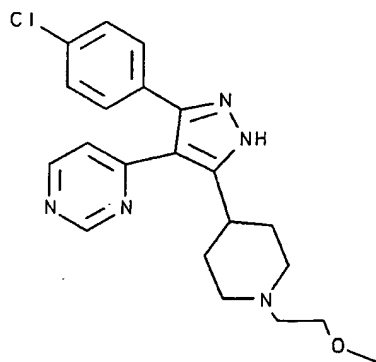


;



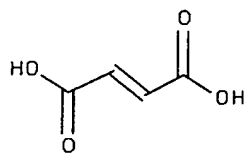
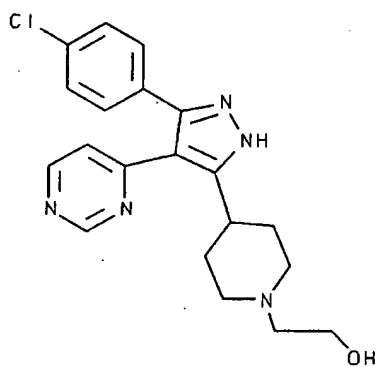
;

1158



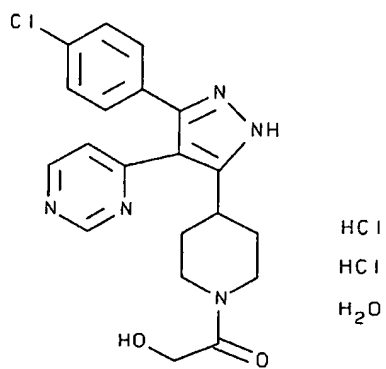
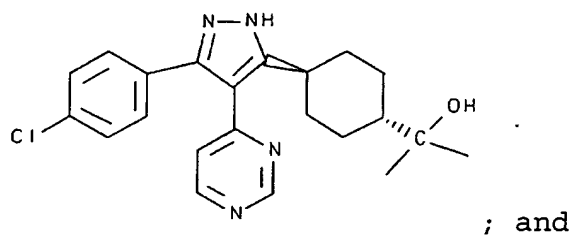
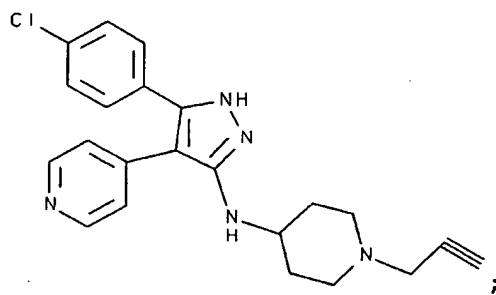
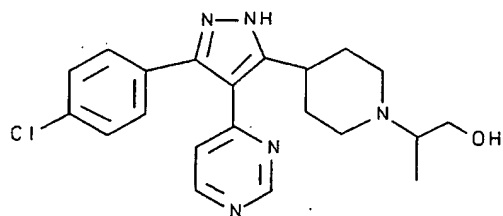
10

;



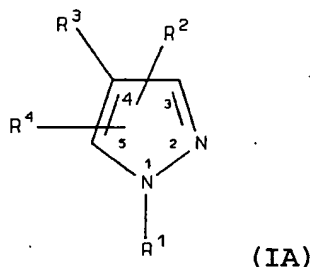
;

1159



1160

126. A compound of Formula IA



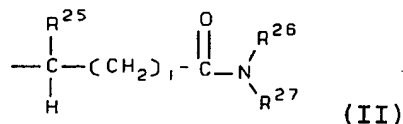
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
- 10    hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene,
- 15    alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
- 20    heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene,
- 25    alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,

1161

- 30 arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

- 35 i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and

- 40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

- R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, 55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, 60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene,

alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or  
R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and



1163

$R^2$  is  $R^{200}$ -cycloalkyl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y-$ ;

-  $C(O)-$ ;

-  $C(O)-(CH_2)_y-$ ;

-  $C(O)-O-(CH_2)_y-$ ;

105 -  $(CH_2)_y-C(O)-$ ;

-  $O-(CH_2)_y-C(O)-$ ;

-  $NR^{202}-$ ;

-  $NR^{202}-(CH_2)_y-$ ;

-  $(CH_2)_y-NR^{202}-$ ;

110 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-$ ;

115 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

-  $O-(CH_2)_y-$ ;

-  $(CH_2)_y-O-$ ;

120 -  $S-$ ; and

-  $O-$ ;

$R^{201}$  represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxy carbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,

1164

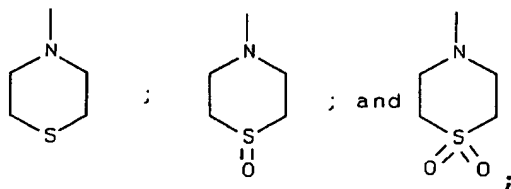
135 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 140 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z is less than or equal to 6; and

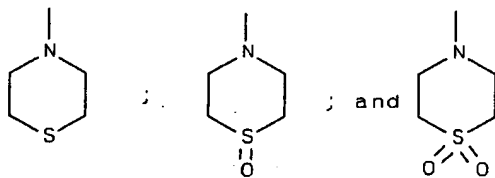
145 x is 0, 1 or 2; and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



150

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



155

groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloaryl amino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,

1165

165 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,  
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
170 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
alkylheterocyclylamino, heterocyclylalkylamino,  
alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
heterocyclylheterocyclylalkylamino,  
175 alkoxycarbonylheterocyclylamino, nitro,  
alkylaminocarbonyl, alkylcarbonylamino,  
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
180 aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
independently selected from halo, alkyl, alkenyl,  
185 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
190 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;

provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
195 ring containing a 2-hydroxy substituent and when  $R^1$  is  
hydrido; and

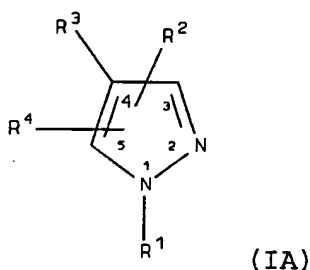
further provided that  $R^4$  is not methylsulfonylphenyl  
or aminosulfonylphenyl; and

further provided that  $R^1$  is not methylsulfonylphenyl;  
200 or

1166

a pharmaceutically-acceptable salt or tautomer thereof.

127. A compound of Formula IA



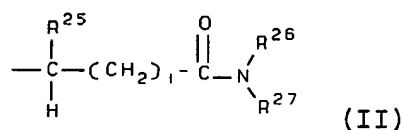
wherein

- 5        R¹ is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene,
- 10
- 15
- 20
- 25

1167

alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

35 i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxy carbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 alkoxy carbonylalkylene, alkoxy carbonyl heterocyclyl,  
 55 alkoxy carbonyl heterocyclyl carbonylalkylene, aminoalkyl,  
 alkylaminoalkylene, arylaminocarbonylalkylene,  
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,  
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
 arylcarbonylalkylene, alkoxy carbonylarylene,  
 60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,

arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or  
R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals

1169

independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is  $R^{200}$ -aryl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y^-$ ;

-  $C(O)-$ ;

-  $C(O)-(CH_2)_y-$ ;

-  $C(O)-O-(CH_2)_y-$ ;

105 -  $(CH_2)_y-C(O)-$ ;

-  $O-(CH_2)_y-C(O)-$ ;

-  $NR^{202}-$ ;

-  $NR^{202}-(CH_2)_y-$ ;

-  $(CH_2)_y-NR^{300}-$ ;

110 -  $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$ ;

-  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y^-$ ;

115 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

-  $O-(CH_2)_y-$ ;

-  $(CH_2)_y-O-$ ; and

120 -  $O-$ ;

$R^{201}$  represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy,

carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,

cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,

125 aralkyl, heterocyclylalkylene, alkylcarbonyl,

hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,

haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,

alkoxycarbonyl, carboxyalkylcarbonyl,

alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,

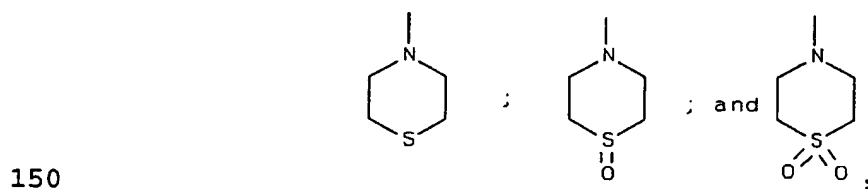
130 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

alkylamino, aralkylamino, alkylaminoalkylene,

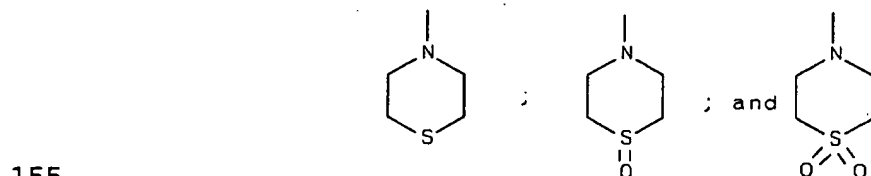
aminocarbonyl, alkylcarbonylamino,

1170

- alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 135 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and  
 140  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and  
 $R^{300}$  is selected from alkyl, aryl and aralkyl; and  
 y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z; and y1 is 1, 2, 3, 4, 5 or 6; wherein y +  
 145 z and y1 + z are less than or equal to 6; and  
 x is 0, 1 or 2; and  
 $R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



- groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 160 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,



1171

alkenylamino, alkynylamino, cycloalkylamino,  
cycloalkenylamino, arylamino, haloarylamino,  
165 heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
alkoxycarbonyl, aryloxycarbonyl, heterocycliloxy carbonyl,  
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
170 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
alkylheterocyclylamino, heterocyclylalkylamino,  
alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
175 heterocyclylheterocyclylalkylamino,  
alkoxycarbonylheterocyclylamino, nitro,  
alkylaminocarbonyl, alkylcarbonylamino,  
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
180 wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
aralkyl; and

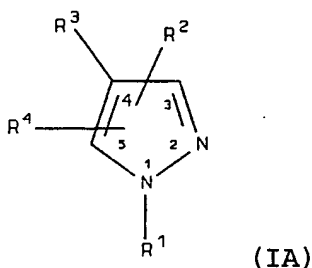
$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
185 independently selected from halo, alkyl, alkenyl,  
alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
190 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminomethylalkylene, aminoalkylamino, and hydroxy;  
195 provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
ring containing a 2-hydroxy substituent and when  $R^1$  is  
hydrido; and

further provided that  $R^4$  is not methylsulfonylphenyl

1172

or aminosulfonylphenyl; and  
 200 further provided that R<sup>1</sup> is not methylsulfonylphenyl;  
 or  
 a pharmaceutically-acceptable salt or tautomer  
 thereof.

128. A compound of Formula IA



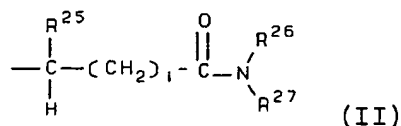
wherein

5 R<sup>1</sup> is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 10 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene,  
 15 alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 20 heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene,

1173

- 25 alkylcarbonylalkylene, arylcarbonylalkylene,  
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

- 35  $i$  is an integer from 0 to 9;  
 $R^{25}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and  
 $R^{26}$  is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxycarbonylalkylene, and alkylaminoalkyl; and  
 $R^{27}$  is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
 55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,  
 alkylaminoalkylene, arylaminocarbonylalkylene,  
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,

1174

- arylaminoacetylalkylene, alkylaminoacetylalkylene,  
arylcarbonylalkylene, alkoxycarbonylarylene,  
60 aryloxyacetylarylene, alkylaryloxyacetylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxyarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminoacetylalkylene,  
aryloxyacetylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or  
R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and

1175

alkoxycarbonylamino; wherein said aryl,

95 heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

- $(CR^{301}R^{302})_y-$ ;

- $C(O)-(CH_2)_{y1}-$ ;

- $C(O)-O-(CH_2)_y-$ ;

- $(CH_2)_y-C(O)-$ ;

105 - $O-(CH_2)_y-C(O)-$ ;

- $NR^{303}-$ ;

- $NR^{303}-(CH_2)_y-$ ;

- $(CH_2)_{y1}-NR^{202}-$ ;

- $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$ ;

110 - $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;

- $S(O)_x-(CR^{202}R^{203})_y-$ ;

- $(CR^{202}R^{203})_y-S(O)_x-$ ;

115 - $S(O)_x-(CR^{202}R^{203})_y-O-$ ;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

- $O-(CH_2)_y-$ ; and

- $(CH_2)_y-O-$ ;

$R^{201}$  represents one or more radicals selected from

120 the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,

125 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene,

1176

- 130 aminocarbonyl, alkylcarbonylamino,  
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino,  
 alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene,  
 135 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

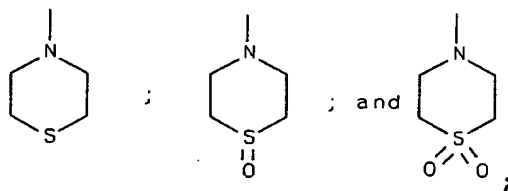
- 140  $R^{301}$  and  $R^{302}$  are independently selected from aryl and  
 aralkyl; and

$R^{303}$  is selected from alkyl, aryl and aralkyl; and

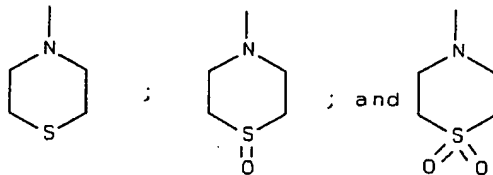
y and z are independently 0, 1, 2, 3, 4, 5 or 6; and  
 y1 is 1, 2, 3, 4, 5 or 6; wherein y + z and y1 + z are  
 145 less than or equal to 6; and

x is 0, 1 or 2; wherein either x or y is other than  
 0 when  $R^{200}$  is  $-S(O)_x-(CR^{202}R^{203})_y-$ ; and

- $R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 150 thiazolylalkyl, thiazolylamino,



- wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 155 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,

1177

- 160 aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, 165 cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxy carbonyl, aryloxy carbonyl, heterocyclyl oxy carbonyl, 170 alkoxy carbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, 175 alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxy carbonyl heterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, 180 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and
- $R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein 185  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, 190 alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxy carbonyl, aryloxy carbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, 195 arylaminoalkylene, aminoalkylamino, and hydroxy;

1178

provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; and

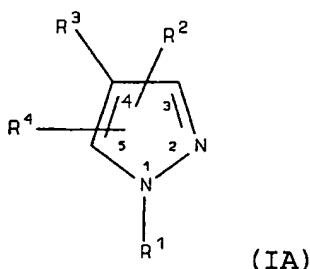
200 further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is hydrido; and

further provided that R<sup>4</sup> is not methylsulfonylphenyl or aminosulfonylphenyl; and

205 further provided that R<sup>1</sup> is not methylsulfonylphenyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

129. A compound of Formula IA



wherein

5 R<sup>1</sup> is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,

10

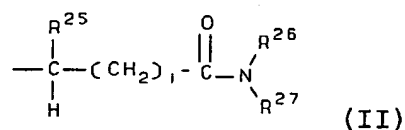
15



1179

- arylsulfinyl, heterocyclysulfinyl, alkylsulfonyl,  
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 20 heterocyclysulfonyl, alkylaminoalkylene,  
 alkylsulfonylalkylene, acyl, acyloxy carbonyl,  
 alkoxycarbonylalkylene, aryloxy carbonylalkylene,  
 heterocyclioxy carbonylalkylene, alkoxycarbonylarylene,  
 aryloxy carbonylarylene, heterocyclioxy carbonylarylene,  
 25 alkylcarbonylalkylene, arylcarbonylalkylene,  
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

- 35 i is an integer from 0 to 9;  
 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and  
 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxycarbonylalkylene, and alkylaminoalkyl; and  
 R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,

alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
aryloxyarylene, aralkoxyarylene,  
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,  
alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminoalkylene, aminocarbonylalkylene,  
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
arylcarbonylalkylene, alkoxycarbonylarylene,  
60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which

they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and

$R^2$  is selected from hydrido, halogen, mercapto, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino, heterocyclylamino, heterocyclylalkylamino, aralkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkylene, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, alkylcarbonylaminoalkylene, aminoalkylcarbonylaminoalkylene, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy, heterocyclylthio, alkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, arylthio, heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl,

1182

alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
 125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,  
 aralkythio, heterocyclylalkylthio, aminoalkoxy,  
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
 130 cycloalkenyl groups may be optionally substituted with  
 one or more radicals independently selected from halo,  
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 aralkyl, heterocyclylalkyl, epoxyalkyl,  
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
 135 haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclylalkylamino,  
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,  
 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 140 cycloalkyl- $R^{201}$  wherein:

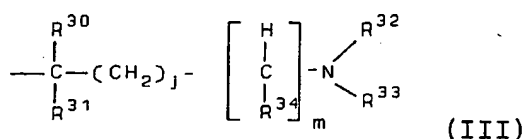
$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y-$ ;
- $C(O)-$ ;
- $C(O)-(CH_2)_y-$ ;
- 145 -  $C(O)-O-(CH_2)_y-$ ;
- $(CH_2)_y-C(O)-$ ;
- $O-(CH_2)_y-C(O)-$ ;
- $NR^{202}-$ ;
- $NR^{202}-(CH_2)_y-$ ;
- 150 -  $(CH_2)_y-NR^{202}-$ ;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;
- 155 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;
- $(CR^{202}R^{203})_y-S(O)_x-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-O-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

1183

- 160        -O-(CH<sub>2</sub>)<sub>y</sub>-;  
           - (CH<sub>2</sub>)<sub>y</sub>-O-;  
           -S-;  
           -O-;  
           or R<sup>200</sup> represents a bond;  
           R<sup>201</sup> represents one or more radicals selected from  
 165    the group consisting of hydrido, halogen, hydroxy,  
          carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,  
          cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
          aralkyl, heterocyclylalkylene, alkylcarbonyl,  
          hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,  
 170    haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,  
          alkoxycarbonyl, carboxyalkylcarbonyl,  
          alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,  
          alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,  
          alkylamino, aralkylamino, alkylaminoalkylene,  
 175    aminocarbonyl, alkylcarbonylamino,  
          alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
          alkylaminoalkylcarbonylamino,  
          aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
          alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 180    alkylimidocarbonyl, amidino, alkylamidino,  
          aralkylamidino, guanidino, guanidinoalkylene, and  
          alkylsulfonylamino; and  
          R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
          alkyl, aryl and aralkyl; and  
 185        y and z are independently 0, 1, 2, 3, 4, 5 or 6  
           wherein y + z is less than or equal to 6; and  
           x is 0, 1 or 2; or  
           R<sup>2</sup> is -NHCR<sup>204</sup>R<sup>205</sup> wherein R<sup>204</sup> is alkylaminoalkylene,  
           and R<sup>205</sup> is aryl; or  
 190        R<sup>2</sup> is -C(NR<sup>206</sup>)R<sup>207</sup> wherein R<sup>206</sup> is selected from  
           hydrogen and hydroxy, and R<sup>207</sup> is selected from alkyl,  
           aryl and aralkyl; or  
           R<sup>2</sup> has the formula:

1184



195        wherein:

      j is an integer from 0 to 8; and

      m is 0 or 1; and

200        R<sup>30</sup> and R<sup>31</sup> are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

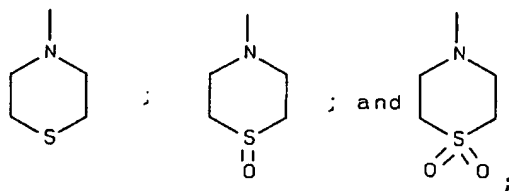
      R<sup>32</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, 205 alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene;

      R<sup>33</sup> is selected from hydrogen, alkyl, -C(O)R<sup>35</sup>, -C(O)OR<sup>35</sup>, -SO<sub>2</sub>R<sup>36</sup>, -C(O)NR<sup>37</sup>R<sup>38</sup>, and -SO<sub>2</sub>NR<sup>39</sup>R<sup>40</sup>, wherein 210 R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup>, R<sup>38</sup>, R<sup>39</sup> and R<sup>40</sup> are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

      R<sup>34</sup> is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

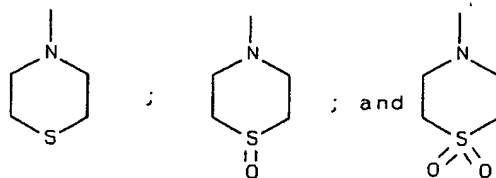
215        R<sup>2</sup> is -CR<sup>41</sup>R<sup>42</sup> wherein R<sup>41</sup> is aryl, and R<sup>42</sup> is hydroxy; and

      R<sup>3</sup> is selected from maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



220        wherein the R<sup>3</sup> maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1185

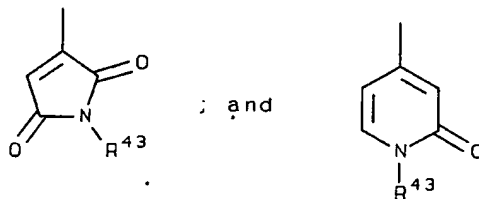


groups may be optionally substituted with one or more  
 225 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 230 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloarylamino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
 235 alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl,  
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
 240 alkylheterocyclylamino, heterocyclylalkylamino,  
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
 heterocyclylheterocyclylalkylamino,  
 alkoxycarbonylheterocyclylamino, nitro,  
 alkylaminocarbonyl, alkylcarbonylamino,  
 245 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR<sup>44</sup>R<sup>45</sup>  
 wherein R<sup>44</sup> is alkylcarbonyl or amino, and R<sup>45</sup> is alkyl or  
 aralkyl; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 250 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 R<sup>4</sup> is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

1186

- 255 alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxy carbonyl, aryloxy carbonyl, haloalkyl, amino, cyano,  
 260 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 provided  $R^3$  is not



(IV)

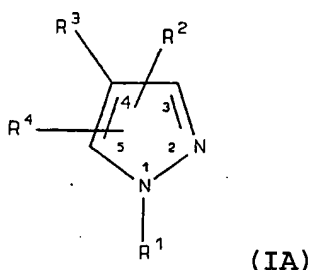
(V)

- 265 wherein  $R^{43}$  is selected from hydrogen, alkyl,  
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
 and  
 further provided  $R^2$  is selected from aryl,  
 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
 270 when  $R^4$  is hydrido; and  
 further provided that  $R^4$  is not methylsulfonylphenyl  
 or aminosulfonylphenyl; and  
 further provided that  $R^1$  is not methylsulfonylphenyl;  
 or  
 275 a pharmaceutically-acceptable salt or tautomer  
 thereof.

130. A compound of Formula IA



1187

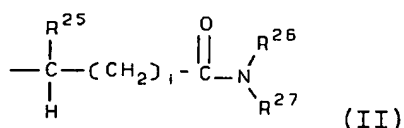


wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula

1188



wherein:

35           i is an integer from 0 to 9;

          R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and  
40 heterocyclcarbonylaminoalkylene; and

          R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

          R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
45 aryl, heterocycl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene,  
50 aralkylheterocycl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyalkylene, alkoxyalkoxyheterocycl,  
55 alkoxyalkoxyheterocyclcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene,  
60 aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxyalkoxyheterocyclarylene, alkoxyalkoxyalkoxyarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

1189

aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-\text{CHR}^{28}\text{R}^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from hydrido, halogen, mercapto,  
100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,  
hydroxyalkyl, aralkyl, alkylheterocyclyl,

1190

heterocyclylalkyl, heterocyclylheterocyclyl,  
heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,  
alkynylamino, arylamino, aryl(hydroxyalkyl)amino,  
105 heterocyclylamino, heterocyclylalkylamino, aralkylamino,  
N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,  
aminoalkylamino, aminocarbonylalkylene,  
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,  
alkylaminoarylene, alkylaminoalkylamino,  
110 alkylcarbonylaminoalkylene,  
aminoalkylcarbonylaminoalkylene,  
alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,  
aminoalkylthio, alkylaminocarbonylalkylthio,  
alkylaminoalkylaminocarbonylalkylthio, alkoxy,  
115 heterocyclylthio, alkylthio, cyanoalkylthio, alkenylthio,  
alkynylthio, carboxyalkylthio, arylthio,  
heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,  
alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,  
alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,  
120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,  
alkoxycarbonylalkyl, alkoxycarbonylalkylamino,  
alkoxycarbonylheterocyclyl,  
alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,  
aralkylthio, heterocyclylalkylthio, aminoalkoxy,  
cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
130 cycloalkenyl groups may be optionally substituted with  
one or more radicals independently selected from halo,  
keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkyl, epoxyalkyl,  
amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
135 haloalkyl, alkylamino, alkynylamino,  
alkylaminoalkylamino, heterocyclylalkylamino,  
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,

1191

arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -

140 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y$ -;

-C(O)-;

-C(O)-(CH<sub>2</sub>)<sub>y</sub>-;

145 -C(O)-O-(CH<sub>2</sub>)<sub>y</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-C(O)-;

-O-(CH<sub>2</sub>)<sub>y</sub>-C(O)-;

-NR<sup>202</sup>-;

-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>y</sub>-;

150 -(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-C(O)-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-(CH<sub>2</sub>)<sub>z</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-NR<sup>203</sup>-(CH<sub>2</sub>)<sub>z</sub>-;

155 -S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-S(O)<sub>x</sub>-;

-S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-O-;

-S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-C(O)-;

-O-(CH<sub>2</sub>)<sub>y</sub>-;

160 -(CH<sub>2</sub>)<sub>y</sub>-O-;

-S-; and

-O-;

or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from

165 the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, 170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

1192

alkylamino, aralkylamino, alkylaminoalkylene,  
 175 aminocarbonyl, alkylcarbonylamino,  
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 180 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

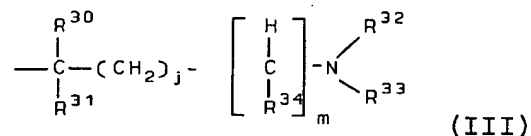
185 y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene,  
 and  $R^{205}$  is aryl; or

190  $R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from  
 hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl,  
 aryl and aralkyl; or

$R^2$  has the formula:



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

$R^{30}$  and  $R^{31}$  are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,  
 200 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and

$R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 205 alkylcarbonylalkylene, arylcarbonylalkylene, and

1193

heterocyclylcarbonylaminoalkylene;

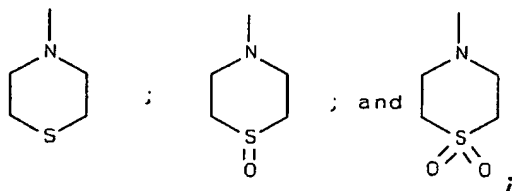
$R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  
 $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ ,  
 wherein

210  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently  
 selected from hydrocarbon, heterosubstituted hydrocarbon  
 and heterocyclyl; and

$R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl,  
 alkylaminocarbonyl, and arylaminocarbonyl; or

215  $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy;  
 and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,

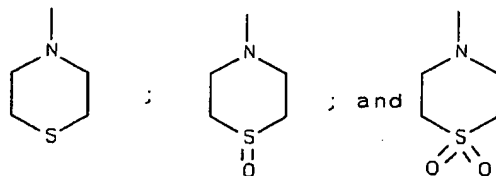


220

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl groups are substituted with one or more radicals  
 independently selected from keto, haloarylamino,  
 225 alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl,  
 alkoxyalkylamino, alkylaminoalkoxy, alkoxyarylamino,  
 alkylsulfonylamino, aryl(hydroxyalkyl)amino,  
 alkylaminoalkylaminoalkylamino, alkylheterocyclylamino,  
 alkylheterocyclylalkylamino,  
 230 heterocyclylheterocyclylalkylamino,  
 alkoxy carbonyl heterocyclylamino and haloalkylsulfonyl;  
 and

wherein the  $R^3$  maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,

1194



235

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxy carbonyl, aryloxy carbonyl, heterocyclyl oxy carbonyl, alkoxy carbonyl amino, alkoxy aryl amino, alkoxy aralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonyl amino, alkylaminoalkyl amino, hydroxyalkyl amino, aralkyl amino, aryl(hydroxyalkyl) amino, alkylaminoalkyl aminoalkyl amino, alkylheterocyclyl amino, heterocyclyl alkyl amino, alkylheterocyclyl alkyl amino, aralkylheterocyclyl amino, heterocyclylheterocyclyl alkyl amino, alkoxy carbonyl heterocyclyl amino, nitro, alkylaminocarbonyl, alkylcarbonyl amino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR<sup>44</sup>R<sup>45</sup> wherein R<sup>44</sup> is alkylcarbonyl or amino, and R<sup>45</sup> is alkyl or aralkyl; and

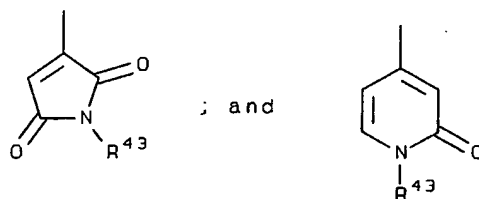
R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

265



1195

- alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 270 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 275 provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
 ring containing a 2-hydroxy substituent and when  $R^1$  is  
 hydrido; and  
 provided  $R^3$  is not



280

(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl,  
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
 and

- further provided  $R^2$  is selected from aryl,  
 285 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
 when  $R^4$  is hydrido; and

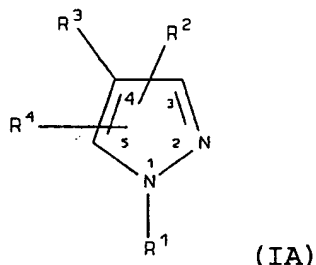
further provided that  $R^4$  is not methylsulfonylphenyl  
 or aminosulfonylphenyl; and

- further provided that  $R^1$  is not methylsulfonylphenyl;  
 290 or

a pharmaceutically-acceptable salt or tautomer  
 thereof.

131. A compound of Formula IA

1196



wherein

- 5         $R^1$  is selected from hydroxy and alkoxyaryl; and  
           $R^2$  is selected from hydrido, halogen, mercapto,  
          alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,  
          hydroxyalkyl, aralkyl, alkylheterocyclyl,  
          heterocyclylalkyl, heterocyclylheterocyclyl,  
 10       heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,  
          alkynylamino, arylamino, aryl(hydroxyalkyl)amino,  
          heterocyclylamino, heterocyclylalkylamino, aralkylamino,  
          N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,  
          aminoalkylamino, aminocarbonylalkylene,  
 15       arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,  
          alkylaminoarylene, alkylaminoalkylamino,  
          alkylcarbonylaminoalkylene,  
          aminoalkylcarbonylaminoalkylene,  
          alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,  
 20       aminoalkylthio, alkylaminocarbonylalkylthio,  
          alkylaminoalkylaminocarbonylalkylthio, alkoxy,  
          heterocyclyoxy, alkylthio, cyanoalkylthio, alkenylthio,  
          alkynylthio, carboxyalkylthio, arylthio,  
          heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,  
 25       alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,  
          alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,  
          carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,  
          alkoxycarbonylalkyl, alkoxycarbonylalkylamino,  
          alkoxycarbonylheterocyclyl,  
 30       alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
          alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
          alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,

aralkythio, heterocyclylalkylthio, aminoalkoxy,  
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 35 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
 cycloalkenyl groups may be optionally substituted with  
 one or more radicals independently selected from halo,  
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 40 aralkyl, heterocyclylalkyl, epoxyalkyl,  
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
 haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclylalkylamino,  
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,  
 45 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y-$ ;
- 50 -C(O)-;
- C(O)-(CH<sub>2</sub>)<sub>y</sub>-;
- C(O)-O-(CH<sub>2</sub>)<sub>y</sub>-;
- 55 - (CH<sub>2</sub>)<sub>y</sub>-C(O)-;
- O-(CH<sub>2</sub>)<sub>y</sub>-C(O)-;
- NR<sup>202</sup>-;
- NR<sup>202</sup>-(CH<sub>2</sub>)<sub>y</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-C(O)-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- 60 - (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-(CH<sub>2</sub>)<sub>z</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-NR<sup>203</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;
- (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-S(O)<sub>x</sub>-;
- S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-O-;
- 65 -S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-C(O)-;
- O-(CH<sub>2</sub>)<sub>y</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-O-;
- S-; and

1198

-O-;

70 or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

90 R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido, alkyl, aryl and aralkyl; and

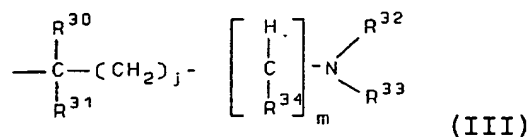
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

95 R<sup>2</sup> is -NHCR<sup>204</sup>R<sup>205</sup> wherein R<sup>204</sup> is alkylaminoalkylene, and R<sup>205</sup> is aryl; or

R<sup>2</sup> is -C(NR<sup>206</sup>)R<sup>207</sup> wherein R<sup>206</sup> is selected from hydrogen and hydroxy, and R<sup>207</sup> is selected from alkyl, aryl and aralkyl; or

100 R<sup>2</sup> has the formula:



1199

wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

105  $R^{30}$  and  $R^{31}$  are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

110  $R^{32}$  is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

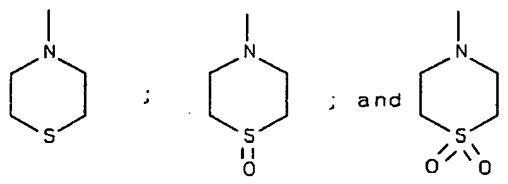
115  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein

$R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

120  $R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

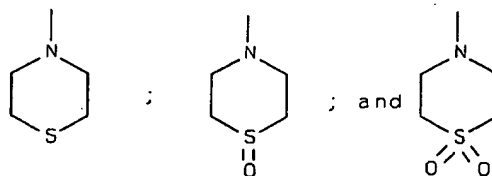
$R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and

125  $R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



130 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1200



groups may be optionally substituted with one or more  
 135 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 140 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloaryl amino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
 145 alkoxycarbonyl, aryloxy carbonyl, heterocyclyl oxycarbonyl,  
 alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino,  
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
 150 alkylheterocyclylamino, heterocyclylalkylamino,  
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
 heterocyclylheterocyclylalkylamino,  
 alkoxycarbonylheterocyclylamino, nitro,  
 alkylaminocarbonyl, alkylcarbonylamino,  
 155 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
 wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
 aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
 160 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

1201

- 165 alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
170 nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;  
provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl  
ring containing a 2-hydroxy substituent and when R<sup>1</sup> is  
hydrido; and  
175 further provided R<sup>2</sup> is selected from aryl,  
heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
when R<sup>4</sup> is hydrido; and  
further provided that R<sup>4</sup> is not methylsulfonylphenyl  
or aminosulfonylphenyl; or  
180 a pharmaceutically-acceptable salt or tautomer  
thereof.

132. A pharmaceutical composition comprising a  
therapeutically-effective amount of a compound, said  
compound selected from the compounds of any one of Claims  
1, 39, 71, 82 and 94, or a pharmaceutically acceptable  
5 salt thereof.

133. A method of treating a TNF mediated disorder,  
said method comprising treating the subject having or  
susceptible to such disorder with a therapeutically-  
effective amount of a compound, said compound selected  
from the compounds of any one of Claims 1, 39, 71, 82 and  
5 94, or a pharmaceutically acceptable salt thereof.

134. A method of treating a p38 kinase mediated  
disorder, said method comprising treating the subject  
having or susceptible to such disorder with a  
therapeutically-effective amount of a compound, said  
compound selected from the compounds of any one of Claims

1202

5 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

135. The method of Claim 134 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid  
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,  
10 inflammatory bowel disease and cachexia.

136. The method of Claim 134 wherein the p38 kinase mediated disorder is inflammation.

137. The method of Claim 134 wherein the p38 kinase mediated disorder is arthritis.

138. The method of Claim 134 wherein the p38 kinase mediated disorder is asthma.

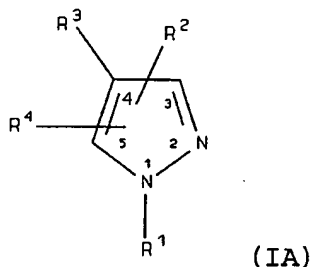
139. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound, said compound selected from the compounds of  
5 any one of Claims 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

140. A method of treating arthritis, said method comprising treating the subject having or susceptible to arthritis with a therapeutically-effective amount of a compound, said compound selected from the compounds of any one of Claims 1, 39, 71, 82 and 94, or a  
5 pharmaceutically acceptable salt thereof.



1203

141. A method of preparing pyrazoles of Formula IA

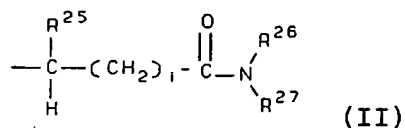


wherein

- R¹ is selected from hydrido, hydroxy, alkyl,
- 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
- 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino,
- 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene,
- 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocyclylloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocyclylloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene,
- 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and
- 30 heterocyclylcarbonyloxyarylene; or

1204

R<sup>1</sup> has the formula



wherein:

i is an integer from 0 to 9;

35 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and

40 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene, 45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene, 50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyarylene, alkoxyheterocycl, alkoxyalkoxyheterocycl, alkoxyalkoxyheterocyclalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene, aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, arylcarbonylarylene, alkylarylcarbonylarylene, 60 alkoxyalkoxyheterocyclarylene, alkoxyalkoxyalkoxyarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene,

cycloalkylthioalkylene, alkylthioarylene,  
65 aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, and alkylaminosulfonylarylene;  
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,  
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
75 independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
80 alkoxyalkylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
and nitro; or  
85 R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
90 alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals may be  
95 optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

R<sup>2</sup> is selected from mercapto,  
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,

1206

100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,  
 aminoalkylcarbonylaminoalkylene,  
 alkylaminoalkylcarbonylamino, aminoalkylthio,  
 alkylaminocarbonylalkylthio,  
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,  
 105 alkenylthio, alkynylthio, carboxyalkylthio,  
 alkoxyalkylthio, alkylsulfinyl, alkylsulfonyl,  
 alkoxyalkyl, alkoxyalkylthio, alkoxyalkylamino,  
 alkoxyalkylaminoalkylene, alkoxyalkylaminoalkoxy,  
 aralkylthio, heterocyclalkylthio, aminoalkoxy,  
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclalkyloxy; or  
 $R^2$  is  $R^{200}$ -heterocyclalkyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- 115 -  $(CR^{202}R^{203})_y-$ ;  
 -  $C(O)-$ ;  
 -  $C(O)-(CH_2)_y-$ ;  
 -  $C(O)-O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-C(O)-$ ;  
 120 -  $O-(CH_2)_y-C(O)-$ ;  
 -  $NR^{202}-$ ;  
 -  $NR^{202}-(CH_2)_y-$ ;  
 -  $(CH_2)_y-NR^{202}-$ ;  
 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;  
 125 -  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;  
 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;  
 130 -  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;  
 -  $O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-O-$ ;  
 -  $S-$ ; and  
 135 -  $O-$ ;

1207

or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, 140 alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, 145 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, 150 aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

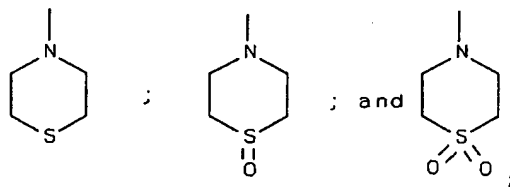
$R^{202}$  and  $R^{203}$  are independently selected from hydrido, alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6 155 wherein y + z is less than or equal to 6; and x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene, and  $R^{205}$  is aryl; or

$R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from 160 hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl, aryl and aralkyl; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

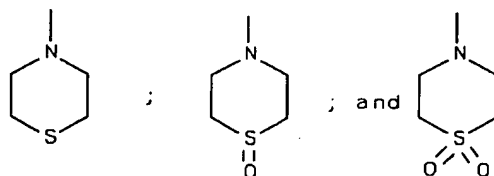


165

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,

1208

thiazolylalkyl, thiazolylamino,



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxy carbonyl, heterocyclyl oxycarbonyl, alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$ , wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio,

200

1209

alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy; or  
210 a pharmaceutically-acceptable salt or tautomer  
thereof,

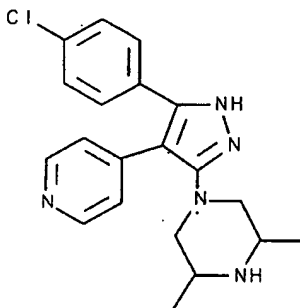
said method comprising the steps of treating a  
substituted ketone with an acyl hydrazide to give the  
pyrazole.

142. The process of Claim 141 wherein the process is  
carried out in an acidic solvent.

143. The process of Claim 141 wherein the acidic  
solvent is acetic acid.

144. The process of Claim 141 wherein the acidic  
solvent is an organic solvent containing an acid.

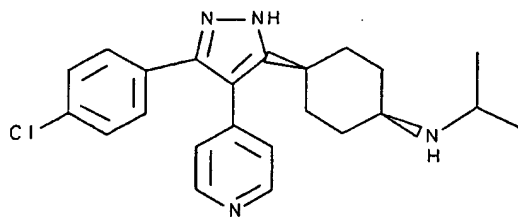
145. The compound:



or a tautomer or pharmaceutically acceptable salt thereof.

1210

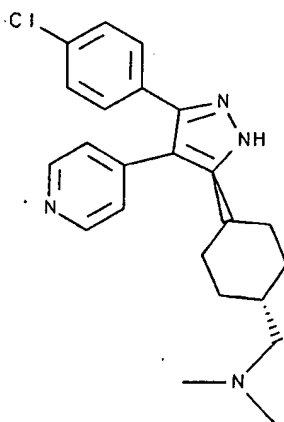
146. A compound of Claim 71 that is:



5

or a tautomer or pharmaceutically acceptable salt thereof.

147. A compound of Claim 39 that is:



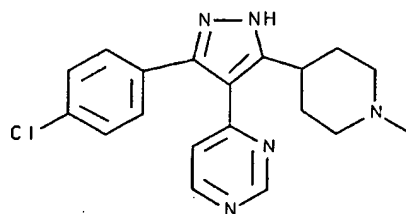
10

or a tautomer or pharmaceutically acceptable salt thereof.

148. The compound:



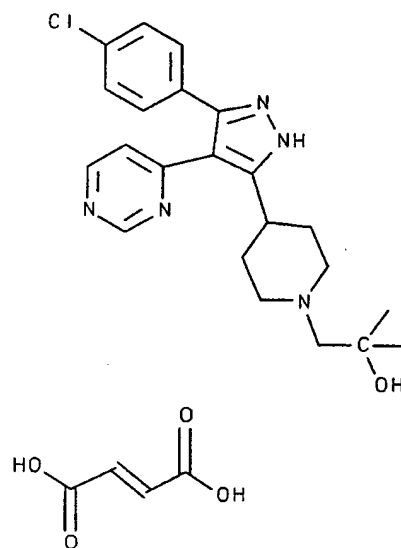
1211



15

or a tautomer or pharmaceutically acceptable salt thereof.

149. A compound of Claim 1 that is:



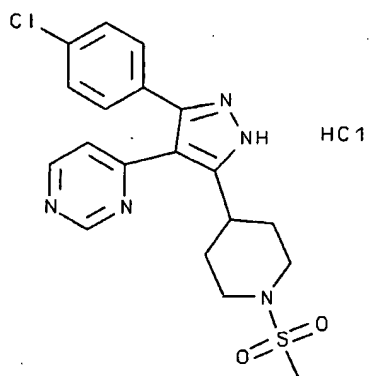
20

or a tautomer or pharmaceutically acceptable salt thereof.

25

150. The compound:

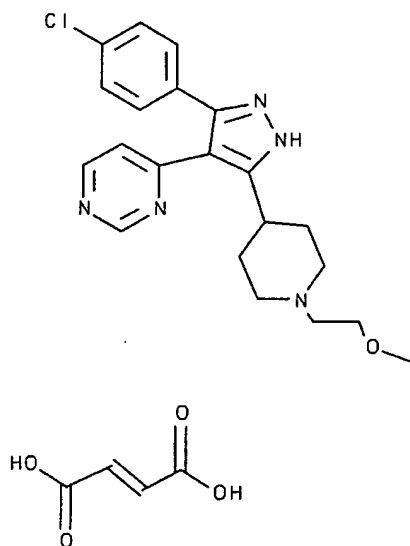
1212



or a tautomer or pharmaceutically acceptable salt thereof.

30

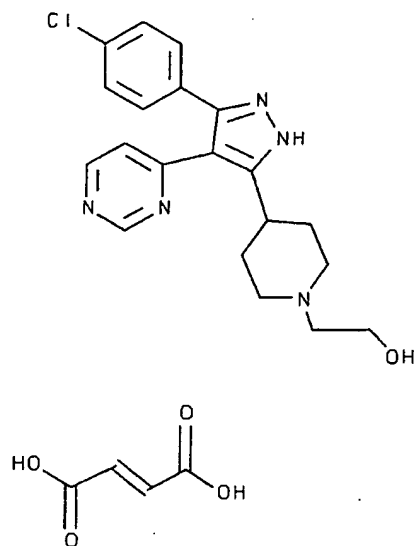
151. A compound of Claim 1 that is:



1213

or a tautomer or pharmaceutically acceptable salt thereof.

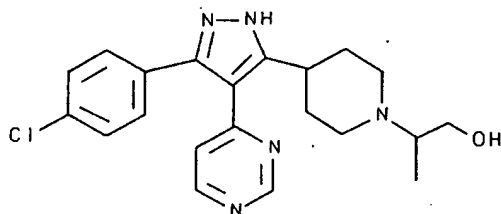
35 152. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

40

153. A compound of Claim 1 that is:

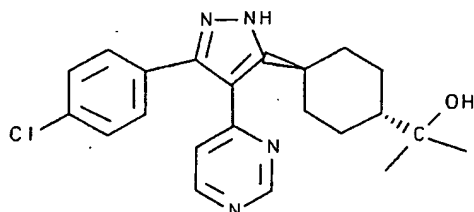


1214

or a tautomer or pharmaceutically acceptable salt thereof.

45

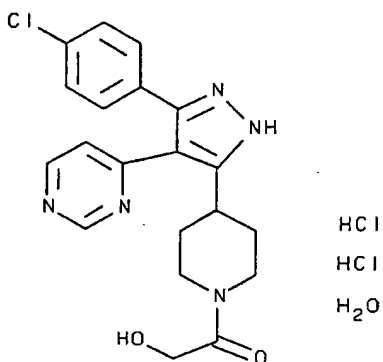
154. A compound of Claim 39 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

50

155. A compound of Claim 1 that is:

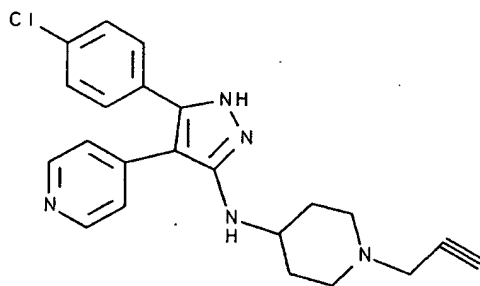


or a tautomer or pharmaceutically acceptable salt thereof.

55

156. A compound of Claim 82 that is:

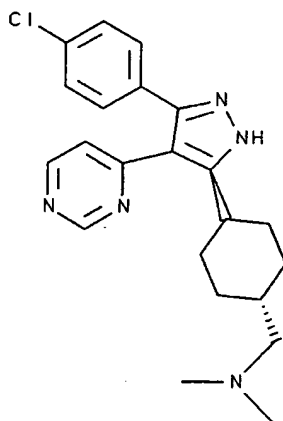
1215



or a tautomer or pharmaceutically acceptable salt thereof.

60

157. A compound of Claim 42 that is:

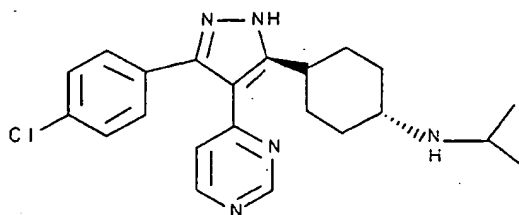


or a tautomer or pharmaceutically acceptable salt thereof.

65

158. A compound of Claim 71 that is:

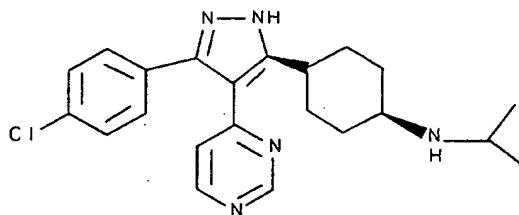
1216



or a tautomer or pharmaceutically acceptable salt thereof.

70

159. A compound of Claim 71 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

75

160. A compound of Claim 70 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US 99/26007

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D401/04 A61K31/415 A61K31/47 A61K31/445 A61K31/44  
A61K31/50 A61K31/505 A61K31/52 C07D405/14 C07D401/14  
C07D409/14 C07D403/04 C07D487/04 C07D473/00 C07D413/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                             | Relevant to claim No.                    |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| X          | WO 96 03385 A (SEARLE & CO ;LEE LEN F (US); PENNING THOMAS D (US); KRAMER STEVEN) 8 February 1996 (1996-02-08) cited in the application abstract; claims 1,8-10; examples 1-15 page 9 -page 73 | 1,39,71,<br>82,93,<br>94,101,<br>126-140 |
| A          | EP 0 846 687 A (LILLY CO ELI) 10 June 1998 (1998-06-10)<br><br>abstract; examples<br>page 21; table 1A<br>page 23 -page 25; table 2A<br><br>-/-                                                | 1,39,71,<br>82,93,<br>94,101             |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 April 2000

Date of mailing of the international search report

18/04/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Paidsdor, B

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/26007

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D417/14 C07D471/04 A61P29/00 //(C07D487/04,293:00,  
231:00),(C07D471/04,221:00,209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                             | Relevant to claim No.        |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| A          | EP 0 846 686 A (PFIZER LTD ;PFIZER (US))<br>10 June 1998 (1998-06-10)<br><br>abstract; claims 1,15<br>page 19; example A24                     | 1,39,71,<br>82,93,<br>94,101 |
| A          | WO 94 19350 A (OKU TERUO ;KAWAI YOSHIO<br>(JP); TANAKA HIROKAZU (JP); FUJISAWA<br>PHARM) 1 September 1994 (1994-09-01)<br>page 53; example 8   | 1,39,71,<br>82,93,<br>94,101 |
| A          | EP 0 531 901 A (FUJISAWA PHARMACEUTICAL<br>CO) 17 March 1993 (1993-03-17)<br><br>abstract<br>pages 49 - 51, preparations<br>page 52; example 1 | 1,39,71,<br>82,93,<br>94,101 |
|            | -/-                                                                                                                                            |                              |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

6 April 2000

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Paisdor, B



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/26007

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                                     |                                              |
|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Category *                                           | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                  | Relevant to claim No.                        |
| A                                                    | DD 295 374 A (STERLING DRUG INC)<br>31 October 1991 (1991-10-31)<br><br>page 7 -page 8; claims; examples                                                                            | 1, 39, 71,<br>82, 93,<br>94, 101             |
| A                                                    | WO 95 31451 A (SMITHKLINE BEECHAM CORP<br>;ADAMS JERRY LEROY (US); GALLAGHER<br>TIMOTHY) 23 November 1995 (1995-11-23)<br><br>page 1 -page 3; claim 1<br>page 16 -page 19; examples | 1, 39, 71,<br>82, 93,<br>94, 101,<br>126-140 |
| P, X                                                 | WO 98 52937 A (ANANTANARAYAN ASHOK<br>;STEALEY MICHAEL A (US); CLARE MICHAEL<br>(US); G) 26 November 1998 (1998-11-26)<br>abstract; claims<br>page 35 -page 49; examples            | 1-160                                        |
| P, X                                                 | WO 98 52940 A (ANANTANARAYAN ASHOK ;CRICH<br>JOYCE ZUOWU (US); SELNESS SHAUN RAJ (US)<br>26 November 1998 (1998-11-26)<br>abstract; claims                                          | 1-160                                        |
| P, X                                                 | WO 98 52941 A (SEARLE & CO ;HANSON GUNNAR<br>J (US); LIAO SHUYUAN (US))<br>26 November 1998 (1998-11-26)<br>abstract; claim 1<br>page 21 -page 24; examples 1, 2                    | 1-160                                        |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/26007

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 133-140  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 133-140  
are directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/26007

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s)                                                                                                                                                                                                 | Publication<br>date                                                                                                                                                                              |
|-------------------------------------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| WO 9603385 A                              | 08-02-1996          | US 5486534 A<br>AU 3126795 A<br>CA 2195123 A<br>EP 0772597 A<br>JP 10503201 T<br>US 5580985 A<br>US 5756530 A<br>US 6028072 A                                                                                              | 23-01-1996<br>22-02-1996<br>08-02-1996<br>14-05-1997<br>24-03-1998<br>03-12-1996<br>26-05-1998<br>22-02-2000                                                                                     |
| EP 0846687 A                              | 10-06-1998          | AU 5365598 A<br>WO 9824437 A<br>US 5972972 A                                                                                                                                                                               | 29-06-1998<br>11-06-1998<br>26-10-1999                                                                                                                                                           |
| EP 0846686 A                              | 10-06-1998          | CA 2223237 A<br>JP 10182614 A                                                                                                                                                                                              | 30-05-1998<br>07-07-1998                                                                                                                                                                         |
| WO 9419350 A                              | 01-09-1994          | AU 681625 B<br>AU 6010894 A<br>CA 2156919 A<br>CN 1120840 A, B<br>EP 0686156 A<br>HU 70832 A<br>IL 108562 A<br>JP 8507056 T<br>MX 9401408 A<br>US 5670503 A<br>ZA 9400787 A                                                | 04-09-1997<br>14-09-1994<br>01-09-1994<br>17-04-1996<br>13-12-1995<br>28-11-1995<br>10-06-1997<br>30-07-1996<br>31-08-1994<br>23-09-1997<br>08-09-1994                                           |
| EP 0531901 A                              | 17-03-1993          | AU 2280592 A<br>CA 2077732 A<br>CN 1070404 A<br>HU 65204 A<br>JP 7252256 A<br>JP 2057962 C<br>JP 6287188 A<br>JP 7088386 B<br>MX 9205145 A<br>US 5478827 A<br>US 5624931 A<br>US 5356897 A<br>ZA 9206417 A<br>CN 1075965 A | 11-03-1993<br>10-03-1993<br>31-03-1993<br>02-05-1994<br>03-10-1995<br>10-06-1996<br>11-10-1994<br>27-09-1995<br>01-04-1993<br>26-12-1995<br>29-04-1997<br>18-10-1994<br>15-03-1993<br>08-09-1993 |
| DD 295374 A                               | 31-10-1991          | NONE                                                                                                                                                                                                                       |                                                                                                                                                                                                  |
| WO 9531451 A                              | 23-11-1995          | US 5559137 A<br>EP 0871622 A<br>JP 10500413 T<br>US 5998425 A                                                                                                                                                              | 24-09-1996<br>21-10-1998<br>13-01-1998<br>07-12-1999                                                                                                                                             |
| WO 9852937 A                              | 26-11-1998          | AU 7698198 A<br>EP 0983260 A<br>NO 995635 A<br>US 5932576 A                                                                                                                                                                | 11-12-1998<br>08-03-2000<br>17-11-1999<br>03-08-1999                                                                                                                                             |
| WO 9852940 A                              | 26-11-1998          | AU 7588398 A<br>NO 995695 A                                                                                                                                                                                                | 11-12-1998<br>21-01-2000                                                                                                                                                                         |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US 99/26007

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| WO 9852941 A                              | 26-11-1998          | AU 7726898 A               | 11-12-1998          |